Immunogenetics (1995) 41: 178–228

Document AT16
Appl. No. 09/458,298

ANNIVERSARY REVIEW

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MHC ligands and peptide motifs: first listing

Received: 13 December 1994

Introduction

The purpose of this article is to provide a compendium of major histocompatibility complex (MHC) peptide motifs and MHC ligands known to date, together with a discussion of the methods used to gain this information. A problem here is the exponential growth of information in this field over the recent years. The number of known MHC ligands was zero in 1989 and three in 1990. This article, written in 1994, lists a couple of hundred such ligands, plus a large number of likely ligands. By the time this work is published, we expect a lot more ligands to be known. On the other hand, the peptide motifs of many of the more important MHC class I molecules are known already, so that this article will still be useful as a source of information. For class II, the situation is a bit different. Only a few allele-specific motifs have been reported, and the data from different authors are partially conflicting. The principles of allele-specific ligand motifs, however, have emerged recently by the combination of information on MHC class II structure, ligand sequencing, and peptide binding assays. Thus, these principles can be applied to further ligands to be identified.

Overview of MHC function

MHC molecules are peptide receptors. Their function is to collect peptides inside the cell and to transport them to the cell surface, where the complex of peptide and MHC molecule may be recognized by the T-cell receptor (TCR) for antigen of T lymphocytes (Rammensee et al. 1993). In normal cells, MHC-associated peptides are derived from normal, that is, self proteins. During their differentiation, T cells become tolerant to complexes of self peptides and self MHC molecules (Von Boehmer 1992). Thus, if any new peptides, e.g., derived from an infectious agent, occur later, they can be recognized by T cells. Since the specific immune system is regulated by T cells, the trimolecular complex of TCR, MHC molecule, and peptide can be considered a control switch for the immune system. Thus, a study of the molecular interactions between the three parts is essential for our understanding of the immune system.

Two classes of MHC molecules are distinguished, class I and class II. Class I molecules consist of a membrane-inserted heavy chain of about 45000 M_r, and a non-covalently attached light chain of 12000 M_r (Klein 1986). The latter is also known as β_2-microglobulin (β_2m). The structure of class I molecules has been resolved by X-ray crystallography (Stern and Wiley 1994). It has some resemblance to a moose's head, whereby the antlers would form a groove that is recognized as a peptide-binding device. HLA-A, B, and C are the "classical" class I molecules of humans, and H-2K, H-2D, and H-2L those of the mouse. Class II molecules are heterodimers consisting of two chains α and β, of similar size (about 30000 M_r), both of which are membrane inserted. HLA-DR, DQ, and DP are the human class II molecules, H-2A and E those of the mouse. Their structure is surprisingly similar to that of class I molecules (Stern and Wiley 1994; Stern et al. 1994; Brown et al. 1993).

All HLA molecules, including the numerous "non-classical", are encoded on chromosome 6, with the exception of β_2m which is on chromosome 15. *H2* genes are on chromosome 17 of the mouse, and the mouse β_2m gene is on chromosome 2.

A peculiarity of MHC genes is their extensive polymorphism, characterized by the presence of dozens or hundreds of alleles in a species. *H2* alleles are designated $H2K^b$, $H2K^d$, $H2K^k$ and so on for class I, and $H2Aa^b$, $H2Aa^k$, $H2Ab^k$, $H2Eb^d$ and so on for class II, whereby different alleles may differ in as many as 40 amino acids (Klein 1986). The present nomenclature (Bodmer et al. 1994) of *HLA* genes and products (which has been changed several times) is outlined as follows: class I heavy chain

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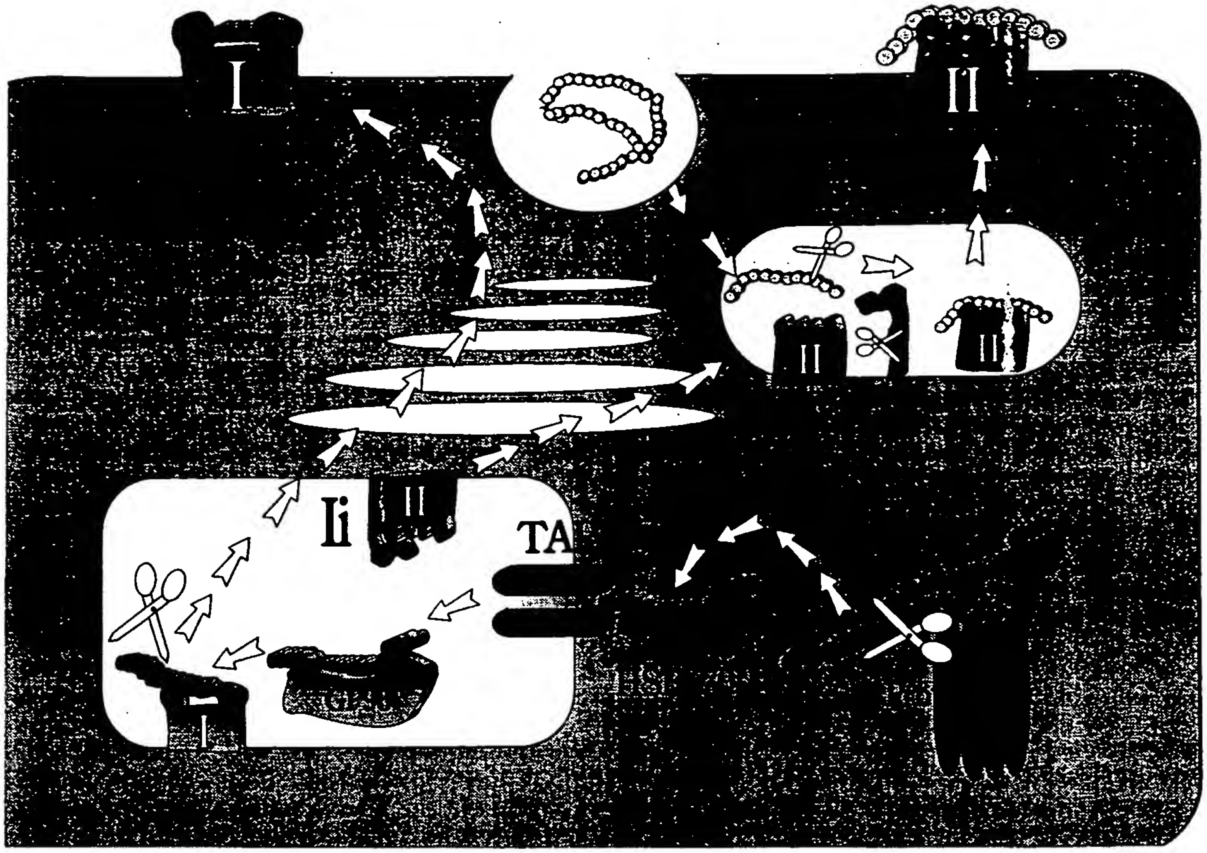

Fig. 1 A simplified and partially hypothetical overview of antigen processing. For explanation see text

loci: *HLA-A*, *B*, and *C*; class II α chain loci: e.g., *HLA-DRA, DQA1, DPA1*, class II β chain loci: e.g., *HLA-DRB1, DRB3, DQB1, DPB1*. Alleles are designated, for example, *HLA-A*0201*, or *HLA-DRB1*0101*. This nomenclature can only be applied if the respective sequences are known. Since this is not the case in many situations, the old designations, e.g., *HLA-A2* or *HLA-DR3*, based on serology, are still being used, and describe collections of alleles with shared serologic determinants (e.g., *HLA-A2* for *A*0201* through *A*02012*). Both class I light chains and HLA-DRα chains are not very polymorphic (Klein 1986). The high (*HLA-B*) or at least moderate polymorphism of the other genes results in the expression of a large number of combinations of alleles at the different loci per chromosome (haplotype), and in a high degree of heterozygosity. Thus each individual has his or her particular combination of HLA molecules, namely up to six different class I and about six different class II molecules (if the non-classical HLA molecules, whose function is not known, are not considered), making it unlikely to find two unrelated individuals with exactly the same combination of *HLA* genes.

A simplified outline of MHC function is given in the diagram in Figure 1. Class I molecules, both heavy and light chains, are synthesized into the ER (reviewed in Jackson and Peterson 1993). The peptides to be loaded on class I molecules are, in many cases, derived from cytosolic proteins. The details of peptide generation are not known definitely. A widely held view, however, is that cytosolic proteins are partially degraded by an endopeptidase activity of the proteasome, a multiunit structure with several activities located in the cytosol (Rock et al. 1994). It is not clear, however, how the products of such endopeptidase activity are related to the final class I ligands (Dick et al. 1994). One possibility is that the proteasomes directly produce the correct ligands. Alternatively, proteasomes could cut out larger peptides requiring further processing. The endopeptidase specificity of the proteasome is such that a protein is cut after hydrophobic or charged residues, in principle. The fine specificity of endopeptidase activity is influenced by two proteasome subunits, LMP2 and LMP7, which are encoded in the MHC region and regulated by IFN. However, the exact kind of LMP influence on specificity is controversial (Howard and Seelig 1993). In any case, such peptides must be transported into the ER lumen by the TAP molecule [(transporter associated with processing) (Neefjes and Momburg 1993)]. According to one hypothesis, these peptides are bound and protected from complete degradation by a chaperone, HSP70, before reaching TAP (Srivastava et al. 1994). Peptide transport by TAP molecules has

been directly demonstrated recently (reviewed in Momburg et al. 1994). Transport has specificity especially regarding the C-termini of peptides, and selectivity for peptide lengths. Peptides of 7 to 23 amino acids have been shown to be transported, whereby optima of 10 to 15 amino acids are seen. Human TAPs do not discriminate much between the C-termini of peptides. In contrast, the mouse TAP has a preference for peptides with hydrophobic C-termini and dislikes peptides with charged termini. This pattern of specificities fits well with the peptide specificities of human and mouse MHC class I molecules, since all mouse class I molecules require peptides with hydrophobic C-termini, whereas some human class I molecules require peptides with basic C-termini. On the other hand, mouse cells transfected with the *HLA-A3* gene, requiring peptide ligands with basic C-termini, can be loaded with the fitting peptides (Maier et al. 1994). This indicates that MHC peptide specificity need not be strictly dependent on TAP specificity. That TAP specificity indeed can influence MHC peptide loading is evident from two different TAP forms in the rat, TAP^a and TAP^u. Dependent on co-expressions of the respective TAP, the peptide spectrum of rat MHC class I molecules, $RT1^u$, is different, as indicated by different HPLC behavior of $RT1^a$-associated peptides. When measured in a peptide transporter assay, TAP^a has the same specificity as human TAP, that is, it does not discriminate between hydrophobic and basic C-termini, whereas TAP^u is more like the mouse transporter, with a preference for peptides with hydrophobic C-termini.

Once they are inside the ER lumen, the further fate of transported peptides is not exactly known. The recently reported physical association of TAP molecules and class I molecules suggested that peptides are directly loaded onto class I molecules immediately after discharge from the transporter (Ortmann et al. 1994; Suh et al. 1994). However, this would require that either the incoming peptides are already of the right size for loading to class I molecules, or that they bind as longer peptides (Falk et al. 1990) and are trimmed while somehow bound to MHC. An alternative hypothesis is that peptides are first bound by a chaperone, gp96, which shuttles the peptides to class I molecules, perhaps with some trimming of peptides underway. The main reason for assuming that gp96 plays a role in antigen processing stems from an impressive series of experiments by Srivastava and co-workers (1994), showing that gp96 molecules are associated with a large array of peptides and are able to immunize mice against antigens presented by MHC class I molecules.

In any event, the peptide somehow reaches the class I molecule and binds into the groove, perhaps after a final trimming step while already in touch with MHC. Unusually long peptides found associated with MHC class I molecules might have escaped such a final trimming (Urban et al. 1994). The assembly sequence of class I heavy chain, β_2m and peptide is not quite clear. A recent report indicates that another chaperone, calnexin, is bound to assembled complexes of heavy chain and β_2m, and thus retains empty class I molecules in the ER (Jackson et al. 1994). It is only upon peptide loading that the fully assembled heavy chain/β_2m/peptide complex is released by calnexin for transportation to the cell surface.

Class II molecules also start their existence in the ER. The two chains, α and β, assemble and are bound by a chaperone-like molecule, the invariant chain [(Ii) (Cresswell 1994)]. This molecule has two functions; one is to direct the α,β-heterodimer to the class II loading compartment, which appears to be a specialized vesicle characterized by the presence of class II molecules. The second function of Ii is the prevention of premature peptide loading to class II molecules. The molecular interactions between Ii and the α,β-heterodimer preventing peptide binding are not completely sorted out; one possibility is an allosteric effect of Ii on the dimer such that the peptide binding groove is closed due to conformational change. The other possibility is that a particular stretch of the invariant chain binds into the groove and thereby competitively prevents the binding of peptides. This latter view is derived from the observation that Ii peptides, called CLIPs (class II-associated invariant chain peptides) are frequently found associated with immunoprecipitated class II molecules, and that CLIPs are especially abundant in cells with a defect in antigen processing. In any case, Ii is removed from the α,β-heterodimer in the class II loading compartment, or shortly before. The peptides loaded onto class II molecules can be derived not only from endocytosed protein but also from protein endogenous to the cells, especially membrane-bound proteins which have a chance to co-localize in the class II loading compartment. Finally, the peptide-loaded α,β-heterodimers are translocated to the cell surface.

The simplified view shown in Figure 1 suggests a strict separation of the processing pathways for class I and class II, respectively. There is strong evidence, however, for considerable cross-talk between the two pathways. Peptides derived from cytosolic proteins, for example, can be loaded onto class II molecules (Pinet et al. 1994). On the other hand, peptides derived from phagocytosed proteins can be loaded onto class I molecules, especially if the phagocytosed protein is aggregated (Pfeifer et al. 1993; Rock et al. 1993). Such side-lines of processing pathways deserve interest because they could be exploited for new strategies of immune intervention.

Methods of characterizing MHC/peptide interactions

The most seminal approach to gain information on the function of MHC molecules as peptide receptors is the X-ray analysis of MHC crystals (Stern and Wiley 1994). The two other principle methods are: 1) Biochemical isolation and study of naturally MHC-associated peptides, and 2) Binding studies with synthetic peptides. The latter two approaches are discussed below:

1) Analysis of natural MHC ligands

The diagram in Figure 2 gives an overview on the approaches used for isolation and analysis of MHC-associated peptides.

The major technical challenge is the small copy number of individual peptides. It is estimated that a cell presents well over 1000 different peptides on its 100000 or so copies of a given MHC allelic product. A few of these peptides are present in high copy number, that is, up to 10000 or more. By far the most ligands, however, occur in a much lower copy number, maybe even down to as low as one copy per cell.

The most sensitive means of detecting isolated peptides is the T-cell assay, which is able to detect peptides in the sub-picomolar range, at least as far as cytotoxic T cells are concerned (Rötzschke et al. 1990). Typically, a peptide-containing sample (e.g., a few µl of an HPLC fraction) is incubated in a total volume of 100 µl together with MHC-expressing, ^{51}Cr-labeled target cells. After some incubation time, e.g., 90 min, CTL are added, the supernatant is harvested 4 to 6 h later, and the relative radioactivity measured indicates the degree of target cell lysis. If the 100 µl volume used for target cell incubation has a concentration of 1 pM, the absolute amount of peptide is 100 attomol, a sensitivity not reached by any other method. The use of the CTL assay, of course, is limited to the detection of T-cell epitopes for which T cells are on hand: Viral antigens, minor H antigens, tumor-associated antigens, transfected model antigens, or antigens recognized by alloreactive T cells. On the other hand, peptide detection assays for class-II-restricted T cells appear to be less sensitive than for class I-restricted T cells.

The major shortcoming of the T-cell assay for peptide detection is that it does not give sequence information. However, the location of a T-cell epitope among HPLC-separated MHC ligands of an infected cell can allow identification of the peptide in combination with biochemical analysis such as Edman degradation or mass spectrometry. The first naturally processed viral T-cell epitopes indeed were identified by the combination of T-cell assay with mass spectrometry, comparison of the HPLC behavior of synthetic and natural peptides, or partially direct sequencing, using radiolabeled amino acids incorporated by virus-infected cells (Rötzschke et al. 1990; van Bleek and Nathenson 1990). A combination of these methods for identification of T-cell epitopes is only possible if the proteins of origin are known. Direct sequencing of HPLC fractions containing a T-cell epitope is rarely successful, namely, only in cases where the T-cell epitope happens to be a peptide highly abundant in that fraction. A marked improvement of sensitivity was brought about by an ingenious combination of HPLC, CTL assay, and mass spectrometry by Cox and co-workers (1994).

By far the most ligands known to date are not T-cell epitopes and these ligands were determined by direct sequencing, either by Edman degradation, or by mass spectrometry, or by a combination of the two methods. Detection limit of Edman degradation is about 1 pmol, that is, the equivalent of 6×10^9 cells for a peptide occurring in 100 copies per cell. Sequencing by tandem mass spectroscopy has been reported to be more sensitive – down to 30 fmol or less. It is, however, challenging to achieve this degree of sensitivity, so that, apart from the pioneering group of Hunt and co-workers (1992), not many other laboratories have come up with similar results.

A special application of Edman degradation is pool sequencing, that is, altogether-sequencing of the complex mixture of peptides eluted from a given MHC species (Falk et al. 1991b). Although disliked by purists, this approach allows one to determine the common characteristics of all peptides associated with a given MHC molecule, with relatively little effort. Pool sequencing of MHC class I ligands led to the discovery of the principle of allele-specific motifs, and allowed a large number of such motifs to be determined. The clear information that can be obtained from pool sequencing of class I ligands is made possible by their uniform length, e.g., 9 amino acids. But even for class II ligands, which can range in length from about 12 to 25 amino acids, pool sequencing is a valuable tool for gaining detailed information on motifs (Falk et al. 1994b).

It appears that the number of amino acids between the N-terminus of class II ligands and the first anchor varies by about three amino acids for the majority of ligands. For DR1, for example, the distance from the N-terminus to the first anchor of the majority of ligands is 5 ± 1 (Falk et al. 1994b). Thus, pool sequencing indicates a cluster at position 4, 5, and 6 for the anchor residues used, aromatic and aliphatic. Again for DR1, the next cluster stretches over

Source of MHC-expressing cells

(tumor cells, transformed cells, cells transfected to express a specific MHC molecule, or fresh or frozen tissue).

↓

Detergent extract

↓

Precipitation of MHC molecules with solid-phase bound antibodies

↓

Dissociation of peptides from MHC molecules with acid (0.1 % TFA or 10 % acetic acid)

↓

Ultrafiltration

↓

Separation of peptides by reversed phase HPLC

↙ ↓ ↘

T cell assay | Edman degradation | Mass spectrometry

Fig. 2 Methods for analysis of MHC ligands

positions 7, 8, and 9, indicating the next anchor for aliphatic residues. The rough motif obtained by such interpretations – absolute position 5 set as relative position 1 to mark the first anchor – can then be complemented and worked out in depth by applying 1) alignment of natural ligands, 2) consideration of the pockets, as revealed recently by crystallography of a monopeptidic DR1 molecule (Stern et al. 1994), and 3) considerations of peptide binding assays. If all four sources of information are considered, a detailed picture of the degenerate (as compared with class I) peptide specificities of class II molecules can be obtained that should be useful for epitope predictions (Friede and coworkers, submitted).

2) Peptide binding assays

MHC/peptide binding assays have a history of leading to obsolete results. On the other hand, with our increasing knowledge of MHC structure and MHC/peptide interaction and specificity, it is possible to design straightforward peptide binding experiments to answer specific questions. A number of approaches can be used to measure peptide binding to MHC. The oldest method is as follows (Buus et al. 1987): MHC molecules are purified and incubated with radioactively labeled peptides. Then the mixture is subjected to a gel filtration column. MHC molecules with the radioactive peptide bound will elute in the exclusion volume, whereas free peptides will elute later. Thus, the amount of radioactivity in the exclusion volume is a measure for peptides bound to MHC. The binding behavior of other, unlabeled peptides can be tested via their capacity to inhibit binding of the radioactive peptide. A number of variations of this method have been used. For example, the radioactive label can be replaced by a fluorescent marker. Furthermore, MHC/peptide complexes can be separated from free peptides by gel electrophoresis, or upon binding of the MHC/peptide complex to solid phase with the help of antibodies. In the latter case, however, two different antibodies reactive with different sites of the MHC molecule are required, one for purification of the MHC molecule, the other for capturing the MHC/peptide complex from the reaction mixture.

Depending on the conditions, these kinds of peptide binding assays can be made very sensitive to detect even low-affinity peptide binding. This may result in problems of interpretations, since low-affinity binding might not be relevant for physiological MHC/peptide interactions.

A second type of binding assay depends on the stabilization of MHC class I molecules by bound peptides. Cells with a defect in antigen processing, for example, TAP-defective RMA-S cells, express only a low density of antibody-detectable MHC class I molecules on their surface, if cultured under normal conditions (37 °C). If such cells are incubated with peptides binding to the expressed class I molecules with high affinity, the latter are stabilized, and their surface density increases (Townsend et al. 1989). Since determination of class I surface density can be easily done by FACS analysis, this approach has been widely used. Since only few cell lines with transporter defects are known, the assay can only be used for MHC molecules expressed by such cells, e. g., H-2K^b or D^b for RMA-S cells. To study peptide binding for additional MHC-molecules, the desired MHC molecule can be expressed in RMA-S or other TAP-defective cells upon gene transfection. The advantage of this MHC-stabilization assay is that it is rather insensitive and thus detects only peptides binding with high affinity that are likely to be physiologically relevant. Stabilization of MHC molecules by peptides can also be measured with purified MHC molecules.

For class II molecules, the binding of high-affinity peptides leads to a compact form of the MHC/peptide complex, as seen by SDS gel electrophoresis, whereas a peptide of lower affinity leads to a "floppy" form of class II molecules.

A very elegant approach for studying the peptide specificity of class II molecules has been developed by Hammer and co-workers (Sinigaglia and Hammer 1994). A peptide library is expressed by bacteriophages. From the peptide-expressing phages only those are selected which are able to bind to a given class II molecule. The peptide sequences expressed by the selected phages are then determined. With this approach, a peptide binding motif of HLA-DR1 has been established that is well reflected among the natural ligands, and can be well explained by the crystal structure of HLA-DR1.

MHC class I ligands and motifs

The main purposes for which this information will be useful are the prediction of T-cell epitopes within proteins of known sequences and the detailed analysis of peptide/MHC interaction. For epitope prediction it is important not to consider just the basic motif of a given MHC molecule, since the non-anchor positions of peptides could also contribute considerably to the interaction with MHC. This is evident from the preferences seen for certain residues at non-anchor-positions in pool sequencing data, from the interaction of such residues with MHC sites as seen in crystals (Madden et al. 1993; Zhang et al. 1992; Fremont et al. 1992), and from detailed binding studies showing that certain residues at a given peptide position can be detrimental for binding (Ruppert et al. 1993; Kast et al. 1994; Parker et al. 1994).

The basic approach to search a protein sequence for an epitope fitting to a given class I molecule is as follows. First, the sequence is screened for stretches fitting to the basic anchor motif (2 anchors in most cases), whereby allowance should be made for some variation in peptide length as well as in anchor occupancy. If a motif, for example, calls for 9mers with I or L at the end, 10mers with a fitting C-terminus should be considered as well, and other aliphatic residues at the C-terminus, like Val or Met, should also be considered. In this way, a list of candidates will be obtained. These are now inspected for having as many non-anchor residues as possible in common with

ligands already known, or with the residues listed among the "preferred residues" or "others" on top of each motif Table. If possible, a binding assay can be performed at this stage to exclude weak binders which occur frequently among peptides conforming to a basic motif. If a detailed study on peptide binding requirements is available, the candidates can also be screened for non-anchor residues detrimental or optimal for binding (Ruppert et al. 1993; Kast et al. 1994; Romero et al. 1991; Ebert et al. 1993). One should keep in mind, however, that pure peptide binding motifs can be misleading in the search for natural ligands, since other constraints, such as enzyme specificity during antigen processing and specificity of transporters or chaperones, are likely to contribute to ligand identity in addition to the MHC binding specificity.

A careful consideration of the pocket structure of the MHC molecule of interest can also be useful for epitope prediction (Falk and Rötzschke 1993). For the P1 residue, for example, preferences can be explained by the residues contributing to the P1 contact site (Falk et al. 1995a,c). Since the MHC residues contributing to the different contact sites can differ among MHC molecules, such considerations should be held with caution, however (Guo et al. 1993). Computer modeling of the MHC molecule in question can be of help here.

The use of allele-specific peptide motifs is limited to a certain extent by exceptional ligands not fitting to a motif, e.g., Frumento and co-workers (1993) and Mandelboim and co-workers (1994). Such ligands will be missed by epitope predictions based on allele-specific motifs. It is not clear as yet how frequently this happens. In most cases, natural ligands will fit to the motifs, whereby substitutions of anchor residues with residues of similar chemistry (e.g., one aliphatic residue for another) and length variations are not infrequent and should be considered. A special case is the mouse H-2M3 molecule. A complete motif is not known, except that this molecule is specialized to present N-formylated peptides of bacterial or mitochondrial origin (Fischer-Lindahl 1991; Shawar et al. 1991).

MHC class II ligands and motifs

The long-awaited X-ray analysis of class II molecules has given us invaluable insight into peptide/class II interactions (Brown et al. 1993; Stern et al. 1994). Especially the detailed information on the 5 DR1-pockets accommodating anchoring side chains of one particular ligand, influenza haemagglutinin 306-318, provided a structural basis for the previously worked out peptide ligand motif of DR1 molecules (Rötzschke and Falk 1994; Sinigaglia and Hammer 1994). Moreover, pocket spacing and structure, as found for this one particular DR1/peptide complex, can be used to deduce the putative interaction for other DR1-peptide complexes and even for some other class II molecules. We found it particularly useful to evaluate pool sequencing data under the aspect of the expected pocket structure (Friede and co-workers, submitted; Schild and co-workers, submitted). Combined with the alignment of individual class II ligands, this approach is a powerful tool to determine allele-specific class II peptide motifs, as we have exercised recently for several closely related DR4 subtypes (Friede and co-workers, submitted).

The general picture for allele-specific class II motifs emerging is as follows. A stretch of nine amino acids, on average starting at absolute positions 3 to 5 of natural ligands, is determined by the respective allele-specific motif, corresponding to the peptide portion embedded in the MHC groove. The first position of this nonamer stretch, P1, represents a hydrophobic anchor for all class II ligand motifs known so far. Anchoring of the hydrophobic P1 side chain in the respective class II pocket appears to be particularly intensive, as impressively illustrated by the deep pocket seen in the monopeptidic DR1 crystal. The importance of P1 side chains is also indicated by the striking influence of P1 on peptide binding, and by the significant clustering of hydrophobic residues at cycles 3 to 5 of self-peptide pools. In addition to P1, several other anchors follow up to P9. For DR1, these are at P4, P6, P7, and P9, as indicated by structural data, whereby the specificity of P7 is somewhat degenerate and escapes detection in binding assays or natural ligand analysis. For several other class II molecules, the same anchor spacing – P1, P4, P6, P7, P9 – is compatible with ligand motif data. DR2, DR3, and DR4 motifs as well as H-2E motifs fall into this category. Other molecules, like DR5, DPw4, and DQ7 appear to have slightly different anchor spacing, e.g., the second anchor at P3, or an anchor at P5. Allele-specific differences can occur at each of the anchor positions, although differences of P1 specificity in HLA-DR molecules are limited by the β86Gly/Val polymorphism. More pronounced allele-specific differences are found for P4, P6, and P9, respectively. Charge differences are particularly evident; P4 of DR17, for example, requires Asp, whereas P4 of DR4Dw10 does not tolerate Asp or Glu but prefers basic or hydrophobic residues. P9, on the other hand, prefers hydrophobic residues for DR1 but negative charges for DR4Dw15 and positive charges for H-2E^k. Interestingly, charge differences in polymorphic stretches of class II molecules (probably reflecting counter charges for charged anchors) have been found to be associated with autoimmune diseases (Gregersen et al. 1987; Khalil et al. 1990; Todd et al. 1987).

Epitope prediction of class II ligands within a protein is not as easy as with class I, because the anchors, or interaction sites, are more degenerate in their specificity. The first step should be to pick out the most allele-specific anchor beyond P1, for example, P4 of DR17, P6 of DR1, or P9 of H-2E^k or DR4Dw15. The selection of nonamer sequences fitting to P1 and the other anchor of the respective motif is then further examined for adherence to the additional anchors. The resulting collection of nonamer stretches might then be inspected for adherence to the putative processing motif XPXX in the flanking regions (Rötzschke and Falk 1994). A quantitative ranking of the contribution of each amino acid residue at almost every position has been determined in an elegant approach by

Hammer and co-workers (1994) for DR4, which led to highly accurate predictions of good DR4 binders.

Technical notes

We have tried to put together all the motifs and natural ligands we were aware of. Due to the flood of data emerging in the past years, however, we anticipate that some information has been overlooked. We apologize in advance to those authors whose work was inadvertently not adequately covered.

In case of those class II ligands occurring as nested sets, we included only one or a few members of the set in many cases.

An X in peptide sequences stands for an undetermined amino acid. However, if the peptide sequence has been determined by mass spectometry, as is the case for the peptides reported by Hunt and co-workers (1992a, b), X stands for either Leu or Ile (which have the same mass). Lowercase letters in peptide sequences indicate residue determination of lower confidence.

As far as T-cell epitopes are concerned, only those have been selected which are likely to be naturally processed; criteria for judgement are to be found in Stevanović and Rammensee (1995). From the numerous class II motifs that have been published, we selected the more convincing ones, that is, those compatible with the class II structure. Due to the variable number of amino acids between the N-terminus and the first anchor of peptides, alignment of ligands or T-cell epitopes to class II motifs is always arbitrary, unless a structural analysis has been performed. For the class II molecules without reasonable motifs, a list of the published ligands is provided, without any attempt at alignment.

If you wish to have your motifs or ligands included in forthcoming listings, please send us reprints (no preprints) of the work describing them. We would also appreciate any comments on errors and omissions, as well as suggestions for improvements.

Acknowledgments The authors gratefully acknowledge the tremendous contributions of Kirsten Falk and Olaf Rötzschke to the original work covered. The original work from our laboratory was supported by grants from the Bundesminister für Forschung und Technologie, the Deutsche Forschungsgemeinschaft (Sonderforschungsbereich 120) and the Leibnizprogramm, and by Hoffman-La Roche Inc., Nutley, N.J. We thank Birgit Stiller and Anne Jordan for preparing the manuscript. The authors wish to thank all those who contributed unpublished and published information.

Table 1 Mouse class I motifs
A H-2K^d

	Position											Source	Ref.
	1	2	3	4	5	6	7	8	9				
Anchor residues		Y							I				a
		F							L				
									V				
Preferred residues			N	P	M	K	T						
			I			F	N						
			L										
Others	K		A	A	V	H	P	H					
	A		H	E	N	I	H	E					
	R		V	S	D	M	D	K					
	S		R	D	I	Y	E	V					
	V		S	H	L	V	Q	F					
	T		F	N	S	R	S	R					
			E		T	L							
			Q		G								
			K										
			M										
			T										
Examples for ligands	T	Y	Q	R	T	R	A	L	V*			Influenza A NP 147–154	b, c
	S	Y	F	P	E	I	T	H	I			Tyrosine kinase JAK1 355–363	a, d
	K	Y	Q	A	V	T	T	T	L*			Tum-P198 14–22	a, e, f
	G	Y	K	D	G	N	E	Y	I*			Lysteriolysin O 91–99	g
	K	Y	G	V	S	V	Q	D	I*			L. monocytogenes p60 217–225	h
	G	Y	L	G	Q	V	T	X	I			Unknown	u
	S	F	V	D	T	R	T	L	L			Collagen 1 α2 4–12	u
T-cell epitopes	L	Y	Q	N	V	G	T	Y	V			Influenza JAP HA 204–212	i
	T	Y	V	S	V	G	T	S	T	L		Influenza JAP HA 210–219	l
	V	Y	Q	I	L	A	I	Y	A			Influenza JAP HA 523–531	i
	I	Y	A	T	V	A	G	S	L			Influenza JAP HA 529–537	i
	T	Y	V	S	V	S	T	S	T	L		Influenza A HA 210–219	k, l
	I	Y	S	T	V	A	S	S	L			Influenza A HA 518–526	k
	R	Y	L	E	N	G	K	E	T	L		HLA-A24 170–179	a, m
	R	Y	L	K	N	G	K	E	T	L		HLA-Cw3 170–179	a, m
	S	Y	I	P	S	A	E	K	I			P. berghei CSP 252–260	n
	S	Y	V	P	S	A	E	Q	I			P. yoelii CSP 281–289	o
	S	Y	I	G	S	I	N	N	I			RSV M2 82–90	p
	D	Y	A	T	L	G	V	G	V			HSV-1 ICP27 448–456	q
	L	Y	R	T	F	A	G	N	P	R	A	HSV-1 ICP27 322–332	q
	T	Y	K	D	T	V	Q	L				Polio VP1 111–118	r
	F	Y	D	G	F	S	K	V	P	L		Polio VP1 208–217	r
	A	Y	I	S	S	G	S	S	T	L		Human Ig VH 49–58	l
	N	Y	D	N	A	G	T	N	L			P. falciparum CSP 39–47	s
	K	Y	L	K	K	I	K	N	S	L		P. falciparum CSP 333–342	s
	K	Y	L	K	I	K	H	L	L			APC frameshift	t

* Also a T-cell epitope

References:
a: Falk et al. 1991 b; b: Rötzschke et al. 1990; c: Falk et al. 1991 a; d: Harpur et al. 1993; e: Sibille et al. 1990; f: Wallny et al. 1992; g: Pamer et al. 1991; h: Pamer 1994; i: Braciale et al. 1987; k: Kuwano et al. 1988; l: Cao et al. 1994; m: Maryanski et al. 1986; n: Romero et al. 1989; o: Weiss et al. 1990; p: Kulkarni et al. 1993; q: Banks et al. 1993; r: Kutubuddin et al. 1992; s: Blum-Tirouvanziam et al. 1994; t: Townsend et al. 1994; u: Reich et al. 1994

Table 1 (Continued)
B H-2D[d]

	Position											Source	Ref.
	1	2	3	4	5	6	7	8	9				
Anchor or auxiliary anchor residues		G	P		R K				I L F				a, b
Other preferred residues				D E Q		N I L	D E						
Examples for ligands	K	G	P	I	T	V	Q	I				Unknown	b
	V	G	P	Q	K	N	E	N	L			Unknown	b
	S	G	P	R	K	X	I	X	L			Homol. mRNA CD40 mouse	b
	A	G	P	D	R	T	E	K	X	L		Unknown	b
	K	G	P	D	K	G	N	E	F			Homol. metalloproteinase 2 inhibitor	b
	I	G	P	E	R	G	H	N	L			Homol. hypoxanthine phosphoribosyl-transferase	b
	D	G	P	V	R	E	H	N	L			Homol. urease canavalia ensiformis	b
	K	G	P	E	R	X	N	G	L			Unknown	b
	S	G	P	E	R	G	E	K	L			Homol. proliferating cell nucleolar antigen P40	b
	D	G	P	V	R	G	I	S	I			Homol. ribosomal protein S17 rat	b
	N	G	P	Q	R	I	Y	N	L			Unknown	b
	S	G	P	V	A	L	V	N	F	I		Unknown	b
	I	G	P	N	R	A	F	N	F			Unknown	b
	S	G	P	E	R	L	L	S	X	Y		Homol. heterog. nucl. RNP complex K	b
	V	G	P	S	G	K	Y	F	I	L		Unknown	b
	F	G	P	Y	K	L	N	R	L			Homol. feline leukemia virus envelope polyprotein	b
	F	G	P	L	K	F	N	V	L	T		Unknown	b
	A	G	P	D	R	F	I	X	X	M		Unknown	b
	F	G	P	Y	R	F	Y	V	L	T		Unknown	b
	S	E	Q	D	L	N	F					Unknown	b
	S	X	H	K	E	Q	P	A	T			Homol. transforming protein spi-1 human	b
	S	X	P	K	T	D	X	Q	T	L		Homol. insulin receptor precursor	b
T-cell epitopes		G	P	P	H	S	N	N	F	G	Y	Tum-P35B 4–13	c
	R	G	P	G	R	A	F	V	T	I		HIV gp160 318–327	d, f
	L	M	G	Y	I	P	L	V	G	A		HCV core 133–142	e

References:
a: Falk and co-workers, unpublished; b: Corr et al. 1993; c: Szikora et al. 1993; d: Takahashi et al. 1988; e: Shirai et al. 1994; f: Bergmann et al. 1993b

Table 1 (Continued)
C H-2L^d

	Position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor residues		**P** S							**F** L M			a, b, c
Other preferred residues			G Q M L	T	T	I K F	F	Q N				
Examples for ligands	Y	**P**	H	F	M	P	T	N	**L***		MCMV pp 89 168–176	d
	L	S	P	F	P	F	D	L*			OGDH 105–112	e
V A I T R I E Q	L	S	P	F	P	F	D	L*			OGDH 97–112	e
	X	**P**	L	E	A	N	Y	Q	X	**F**	Unknown	c
	A	**P**	Q	P	G	M	E	N	**F**		Unknown	c
	Q	**P**	Q	R	G	R	E	N	**F**		Unknown	c
	X	**P**	Q	P	G	R	E	Q			Unknown	c
	X	**P**	Q	P	N	L	Y	Q	**L**		Unknown	c
	X	**P**	A	X	A	Y	P	Y			Unknown	c
	Y	**P**	N	V	N	I	H	N	**F**		Unknown	c
	X	**P**	Q	K	A	G	G	F	L	**M**	Phosphoglycerate kinase 180–189	c
T-cell epitopes	R	**P**	Q	A	S	G	V	Y	**M**		LCMV NP 118–126	f, g
	I	S	T	Q	N	H	R	A	**L**		Tumor antigen P91A 12–20	h
	L	**P**	Y	L	G	W	L	V	**F**		Tumor antigen P815 35–43	i
	A	**P**	T	A	G	A	F	F	**F**		JHMV Nucleocapsid 318–326	k
	Y	**P**	A	L	G	L	H	E	**F**		Measles NP 281–289	l
	T	**P**	H	P	A	R	I	G	**L**		E. coli β-gal. 876–884	m
	D	**P**	V	I	D	R	L	Y	**L**		Measles HA 343–351	n
	S	**P**	G	R	S	F	S	Y	**F**		Measles HA 544–552	n

* Also a T-cell epitope

References:
a: Falk et al. 1991 b; b: Falk and co-workers, unpublished; c: Corr et al. 1992; d: Reddehase et al. 1989; e: Udaka et al. 1992; Udaka et al. 1993; f: Whitton et al. 1989; g: Schulz et al. 1991; h: Lurquin et al. 1989; i: Lethé et al. 1992; k: Bergmann et al. 1993 a; l: Beauverger et al. 1993; m: Gavin et al. 1994; n: Beauverger et al. 1994

Table 1 (Continued)
D H-2K^b

	Position										Source	Ref.
		1	2	3	4	5	6	7	8			
Anchor or auxiliary anchor residues				Y		F			L			a
						Y			M			
									I			
									V			
Other preferred residues		R	N	P	R		T	N				
		I			D		I	Q				
		L			E		E	K				
		S			K		S					
		A			T							
Examples for ligands		R	G	Y	V	Y	Q	G	L*		VSV NP 52–59	b
		S	I	I	N	F	E	K	L*		Ovalbumin 258–276	a, c, d
		H	I	Y	E	F	P	Q	L		Unknown	n
T-cell epitopes		I	I	Y	R	F	L	L	I		Rotavirus VP7 33–40	e
		S	S	I	E	F	A	R	L		HSV glycoprotein B 498–505	f
	F	A	P	G	N	Y	P	A	L		Sendai virus NP 324–332	g, h
		K	S	P	W	F	T	T	L		MuLV p15E 574–581	i, k
		V	G	P	V	F	P	P	G	M	Rotavirus VP6 376–384	l
	Y	S	G	Y	I	F	R	D	L		Rotavirus VP3 585–593	l
		F	E	Q	N	T	A	Q	A+		MUT 2 tumor antigen	m
		F	E	Q	N	T	A	Q	P+		MUT 1 tumor antigen	m

* Also a T-cell epitope
\+ One of these peptides was found in a total cell extract of K^b-expressing tumor cells

References:
a: Falk et al. 1991 b; b: van Bleek and Nathenson 1990; c: Rötzschke et al. 1991; d: Carbone et al. 1988; e: Franco et al. 1993; f: Bonneau et al. 1993; g: Kast et al. 1991; h: Schumacher et al. 1991; i: Sijts et al. 1994; k: White et al. 1994; l: Franco et al. 1994; m: Mandelboim et al. 1994; n: Wallny 1992

Table 1 (Continued)
E H-2D^b

	Position											Source	Ref.
	1	2	3	4	5	6	7	8	9				
Anchor residues					N				M				a
									I				
Preferred residues		M	I	K		L							
			L	E		F							
			P	Q									
			V	V									
Others	A	A	G	D		A	D	F					
	N	Q		T		Y	E	H					
	I	D				T	Q	K					
	F					V	V	S					
	P					M	T	Y					
	S					E	Y						
	T					Q							
	V					H							
						I							
						K							
						P							
						S							
Examples for ligands	A	S	N	E	N	M	E	T	M*			Influenza A34 NP 366–374	a, b, c
	I	Q	V	G	N	T	R	T	I*			Yersinia YOP 51 249–257	n
T-cell epitopes	A	S	N	E	N	M	D	A	M			Influenza A68 NP 366–374	d
	S	A	I	N	N	Y	A	Q	K	L		SV 40 T 206–215	e, o
	C	K	G	V	N	K	E	Y	L			SV 40 T 223–231	e, o
	Q	G	I	N	N	L	D	N	L			SV 40 T 489–497	e, o
	S	G	P	S	N	T	P	P	E	I		Adenovirus 5 E1A 234–243	f
	F	Q	P	Q	N	G	Q	F	I			LCMV NP 396–404	g
	S	G	V	E	N	P	G	G	Y	C	L	LCMV GP 276–286	h
	K	A	V	Y	N	F	A	T	C	G		LCMV GP 33–42	i, k
	R	A	H	Y	N	I	V	T	F			HPV16 E7 49–57	l
	N	N	L	D	N	L	R	D	Y	(L)		SV 40 T 492–500 (501)	m

* Also a T-cell epitope

References:
a: Falk et al. 1991b; b: Rötzschke et al. 1990; c: Townsend et al. 1986; d: Cerundolo et al. 1991; e: Deckhut et al. 1992; f: Kast et al. 1989; g: Yanagi et al. 1992; h: Oldstone et al. 1988; i: Oldstone et al. 1993; k: Klavinskis et al. 1990; l: Feltkamp et al. 1993; m: Alsheikly 1994; n: Stambach and Bevan 1994; o: Tevethia et al. 1990

Table 1 (Continued)

F H-2K^k

	Position 1	2	3	4	5	6	7	8	9	Comments	Ref.
Anchor residues		E						I	I	C-terminus at P8 or P9	a, b, c
Preferred residues	V	D	K	L	A	N	T				
	F		N		G	K					
			Y		P	H					
			M		T						
			Q		V						
			I		F						
			L		S						
			F								
			P								
			H								
			T								
										Source	
Examples for natural ligands	H	E	T	T	F	N	S	I		β Actin 275–282	k
	D	D	H	R	A	G	K	I		S24 ribosomal protein 53–60	k
	Y	E	D	T	G	K	T	I		Unknown	k
	K	E	M	K	A	K	V	I		Homol. T cell transcript. factor 1	k
	E	E	E	P	V	K	K	I		Hn RNP C protein 84–91	k
	S	E	I	V	G	K	R	I		S7/S8 ribos. protein 137–144	k
	S	E	G	G	S	H	T	I		H-2D^k 112–119	k
	D	E	R	T	V	R	K	I		Unknown	k
	E	E	D	P	V	K	K	V		CArG bind. factor A 209–216	k
	E	A	Y	L	G	K	K	V		BiP 158–165	k
T-cell epitopes	F	E	A	N	G	N	L	I		Influenza A HA 259–266	c, i
	I	E	G	G	W	T	G	M	I	Influenza A HA 10–18	c, i
	S	D	Y	E	G	R	L	I		Influenza A NP 50–57	d, l
	F	E	S	T	G	N	L	I		Influenza JAP HA 255–262	e
	S	E	F	L	L	E	K	R	I	SV 40 T 560–568	f
	Y	E	N	D	I	E	K	K	I	P. falciparum CSP 375–383	g
	D	E	L	D	Y	E	N	D	I	P. falciparum CSP 371–379	g
	T	E	M	E	K	E	G	K	I	HIV-1 RT 206–214	h
	V	E	A	E	I	A	H	Q	I	Rabies NS 197–205	i
	E	E	G	A	I	V	G	E	I	Influenza A NSI 152–160	a

References:
a: Cossins et al. 1993; b: Norda et al. 1993; c: Gould et al. 1991; d: Bastin et al. 1987; e: Sweetser et al. 1989; f: Rawie et al. 1988; g: Kumar et al. 1988; h: Hosmalin et al. 1990; i: Larson et al. 1991; Gould et al. 1987; k: Brown et al. 1994; l: Gould et al. 1989

G H-2K^kml

	Position 1	2	3	4	5	6	7	8	Source	Ref.
Anchor or auxiliary anchor residues		E						I		a
Other preferred residues		Q	K	P	A		R			
		G	N		R		Y			
		P	Q		K					
			G							
			M							
			P							
			Y							

References:
a: Norda et al. 1993

Table 1 (Continued)

H Qa-2

	Position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor or auxiliary anchor residues		M	N		V	K	H		L			a, b
		L	I		I	M			I			
		Q	L			I			F			
Other preferred residues	K		T	P	L	L	R	E				
	A			E	T	F		Q				
	E			A	E	N		N				
	Q			G	H	Y		D				
				K	M			K				
				S	F			S				
				D	Y			T				
								R				
Examples for ligands	K	Q	N	P	I	A	H	Q	L		Unknown	b
	A	L	A	E	L	P	H	E	L		Unknown	b
	K	Q	N	P	T	V	H	H	L		Unknown	b
	A	G	L	L	G	M	R	S	G	L	Unknown	b
	K	L	I	K	V	Y	H	S	L		Unknown	b
	V	Q	N	X	T	M	H	P	I		Unknown	b
	R	S	N	G	Q	V	H	M	L		Unknown	b
	K	L	T	G	I	K	H	E	L		Cofilin 127–135	b
	A	M	L	A	T	Y	H	K	L		Unknown	b
	G	Q	L	X	V	X	H	K	L		Unknown	b
	I	L	M	E	H	I	H	K	L		Ribosomal protein L19 137–145	b
	A	Q	N	P	V	L	Y	Q	I		Unknown	b
	S	L	I	K	T	V	R	E	M		Unknown	b
	K	M	L	P	V	E	H	N	L		Unknown	b
	K	Q	L	I	V	T	Y	H	L		Unknown	b
	S	V	L	D	D	L	A	L	L		Unknown	b
	Y	E	S	P	L	M	X	F	L		Unknown	b
	D	L	L	G	T	L	H	N	L		Unknown	b

References:
a: Rötzschke et al. 1993; b: Joyce et al. 1994

I Selected other T-cell epitopes

MHC	Sequence													Comments	Ref.
H-2D^k		R	R	K	G	K	Y	T	G	L				T cell epitope of LEC-A	a
H-2M3	fM		F	F	I	N	I	L	T	L	L	V	P	ND1α 1–17	b
	fM		F	F	I	N	A	L	T	L	L	V	P	ND1β 1–17	b

References:
a: de Bergeyck et al. 1994; b: Fischer Lindahl 1991

Table 2 HLA-A motifs
A HLA-A1

	Position													Source	Ref
	1	2	3	4	5	6	7	8	9						
Anchor or auxiliary anchor residues		T	D	P			L		Y						a, b, c,
		S	E												f, i
Other preferred residues		L		G	G	G									
				I	N	V									
					Y	I									
Examples for ligands	A	T	D	F	K	F	A	M	Y					Cyclin-like protein 135–143	a, i
	I	A	D	M	G	H	L	K	Y					Proliferation cell nuclear antigen 241–249	a, b, i
	M	I	E	P	R	T	L	Q	Y					Ribosomal protein S16 40–48	a, b
	Y	T	S	D	Y	F	I	S	Y					Ets-1 154–162	a, i
	L	T	D	P	G	V	L	D	Y					Unknown	a
	V	S	D	I	V	G	P	D	G	L	V	Y		Fibrillarin 177–188	a, b
	Y	T	D	Y	G	G	L	I	F	N	S	Y		Cytochrome C oxidase II	a, i
	Q	S	E	D	G	S	H	T	I	Q	I	M	Y	HLA class I α chain 111–123	a
	Y	L	D	D	P	D	L	K	Y					Cytosine methyl transferase 238–246	i
	S	T	D	H	I	P	I	L	Y					Fructose-6-amino transferase 217–225	i
	D	S	D	G	S	F	F	L	Y					IgG4 279–287	i
	G	T	D	E	X	R	N	X	Y					Unknown	i
	V	S	D	P	Y	N	X	K	Y					Unknown	d, i
	V	A	D	K	V	H	X	M	Y					Unknown	i
	Y	T	A	V	V	P	L	V	Y					J-chain 102–110	i
	Y	T	N	P	Q	F	N	V	Y					Unknown	i
	E	T	X	X	P	D	W	S	Y					Unknown	i
	F	T	D	V	N	S	X	X	R	Y				Unknown	i
	S	S	E	Q	T	F	M	Y	Y					Ornithine decarboxylase 309–317	b
	S	T	E	P	V	N	I	L	Y					Unknown	b
	G	T	D	P	G	V	L	I	Y					Unknown	b
	S	T	E	P	P	M	L	N	Y					Unknown	b
	S	L	E	P	Q	R	T	Q	Y					Unknown	b
	F	T	E	V	S	I	R	K	Y					Unknown	b
	K	F	D	P	V	N	L	V	Y					Unknown	b
	A	V	D	P	G	G	M	Y	S					Unknown	b
	F	G	S	G	A	R	D	X	Y					Unknown	b
	Y	X	E	P	Q	F	L	T	Y					Unknown	b
	A	X	I	P	A	F	I	N	Y					Unknown	b
	I	T	E	D	M	G	H	L	K	Y				Unknown	f
	E	T	D	X	X	X	D	R	S	E	Y			Unknown	i
T-cell epitopes	E	A	D	P	T	G	H	S	Y					MAGE-1 161–169	e, k
	V	S	D	G	G	P	N	L	Y					Influenza A PB1 591–599	b, f
	C	T	E	L	K	L	S	D	Y					Influenza A NP 44–52	f
	E	V	D	P	I	G	H	L	Y					MAGE-3	g, h

References:
a: Falk et al. 1994c; b: Di Brino et al. 1993b; c: Sette et al. 1994; d: Engelhard 1994; e: Traversari et al. 1992; f: DiBrino et al. 1994; g: Gaugler et al. 1994; h: Celis et al. 1994; i: Kubo et al. 1994; k: Van der Bruggen et al. 1991

Table 2 (Continued)
B HLA-A*0201

		Position														Source	Ref.
		1	2	3	4	5	6	7	8	9							
Anchor or auxiliary anchor residues			L				V			V							a
			M							L							
Preferred residues					E				K								
					K												
Other residues		I		A	G	I	I	A	E								
		L		Y	P	K	L	Y	S								
		F		F	D	Y	T	H									
		K		P	T	N											
		M		M		G											
		Y		S		F											
		V		R		V											
						H											
Examples for ligands		S	L	L	P	A	I	V	E	L						Protein phosphatase 2A 389–397	b
		Y	L	L	P	A	I	V	H	I						ATP-dependent RNA Helicase 148–156	b
		T	L	W	V	D	P	Y	E	V						B-cell transloc. gene 1 protein 103–111	b
		S	X	P	S	G	G	X	G	V						Unknown	b
		G	X	V	P	F	X	V	S	V						Unknown	b
		S	X	X	V	R	A	X	E	V						Unknown	b
		K	X	N	E	P	V	X	X	X						Unknown	b
		A	L	W	G	F	F	P	V	X+						Unknown mouse protein	b, e
		L	L	D	V	P	T	A	A	V						IP-30 signal sequence 27–35	b
	L	L	L	D	V	P	T	A	A	V						IP-30 signal sequence 26–35	b, c
	L	L	L	D	V	P	T	A	A	V	Q	A				IP-30 signal sequence 26–37	b, c
	L	L	L	D	V	P	T	A	A	V	Q					IP-30 signal sequence 26–36	c
		V	L	F	R	G	G	P	R	G	L	L	A	V	A	SSR α signal sequence 12–25	d, c
		M	V	D	G	T	L	L	L	L						HLA-E signal sequence 1–9	b
		Y	M	N	G	T	M	S	Q	V+						Tyrosinase 369–377	f, g, h, i
		M	L	L	S	V	P	L	L	L	G					Calreticulin signal sequence 1–10	c
		S	L	L	G	L	L	V	E	V*						Unknown	l
		A	L	L	P	P	I	N	I	L*						Unknown	l
		T	L	I	K	I	Q	H	T	L*						Unknown	l
		A	L	I	V	G	X	N	D	D*						Unknown	l
		H	L	I	D	Y	L	V	T	S*						Carboxypeptidase M 91–99	l
		I	L	A	P	P	V	V	K	L	L	V*				Unknown	l
		A	L	F	P	Q	L	V	I	L*						Unknown	l
		G	I	L	G	F	V	F	T	L+						Influenza matrix protein 58–66	a, k, o, y, z
T-cell epitopes		I	L	K	E	P	V	H	G	V						HIV-1 RT 476–484	a, e, j
		I	L	G	F	V	F	T	L	T	V					Influenza matrix protein 59–68	a, k
		L	L	F	G	Y	P	V	Y	V						HTLV-1 tax 11–19	o
		G	L	S	P	T	V	W	L	S	V					Hepatitis B sAg 348–357	m
		W	L	S	L	L	V	P	F	V						Hepatitis B sAg 335–343	m
		F	L	P	S	D	F	F	P	S	V					Hepatitis B Nucleocapsid 18–27	n
		C	L	G	G	L	L	T	M	V						EBV LMP2 426–434	p
		F	I	A	G	N	S	A	Y	E	Y	V				HCMV glycoprotein B 618–628	m
		K	L	G	E	F	Y	N	Q	M	M					Influenza B NP 85–94	q
		K	L	V	A	L	G	I	N	A	V					HCV-1 1406–1415	r
		D	L	M	G	Y	I	P	L	V						HCV core 132–140	s
		R	L	V	T	L	K	D	I	V						HPV 11 E7 4–12	t
		M	L	L	A	L	L	Y	C	L						Tyrosinase 1–9	f, g
		A	A	G	I	G	I	L	T	V						Melan A/Mart 1	w, x
		Y	L	E	P	G	P	V	T	A						pmel 17/gp100	u
		I	L	D	G	T	A	T	L	R	L					pmel 17/gp100	v

* Class I ligands allocated to A2 by motif. + Also a T-cell epitope

References:
a: Falk et al. 1991 b; b: Hunt et al. 1992; c: Henderson et al. 1992; d: Wei and Cresswell 1992; e: Henderson et al. 1993; f: Wölfel et al. 1994; g: Robbins et al. 1994; h: Brichard et al. 1993; i: Engelhard et al. 1993; j: Walker et al. 1989; k: Gotch et al. 1988; l: Harris et al. 1993; m: Nayersina et al. 1993; n: Bertoletti et al. 1993, 1994; o: Utz et al. 1992; p: Lee et al. 1993; q: Robbins et al. 1989; r: Chisari and co-workers, personal comm.; s: Shirai et al. 1994; t: Tarpey et al. 1994; u: Cox et al. 1994; v: Kawakami et al. 1994 b; w: Coulie et al. 1994; x: Kawakami et al. 1994 a, c; y: Falk et al. 1994 a; z: Bednarek et al. 1991

Table 2 (Continued)
C HLA-A*0205

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		V				I			L		a
		L				V					
		I				L					
		M				A					
Other preferred residues		Q	Y	G	Y	T	Q	K			
			P	E	V						
			F	D	L						
			I	K	I						
				N							

References:
a: Rötzschke et al. 1992

D HLA-A3

	Position											Source	Ref.
	1	2	3	4	5	6	7	8	9	10			
Anchor or auxiliary anchor residues		L	F			I	I		K	K			a, b, g
		V	Y			M	L		Y				
		M				F	M		F				
						V	F						
						L							
Other preferred residues	I				I	T		Q					
					P			S					
					V			T					
					K			K					
Examples for ligands	K	X	F	K	M	I	L	R	K			Unknown	a
	K	L	F	K	N	I	L	Y	K			Unknown	a
	Y	L	X	V	R	X	A	X	i	V		Unknown	a
	K	L	H	K	Q	R	A	K	S			Unknown	a
	S	L	F	K	Q	V	V	T	K			Unknown	a
	K	X	F	V	K	X	L	X	Y			Unknown	a
	S	L	F	N	T	H	L	X	K			Unknown	a
	T	L	A	N	D	X	V	V	P			Unknown	a
	G	I	F	A	X	X	X	V	K	A		Unknown	a
	T	X	F	V	K	X	L	X	Y			Unknown	a
	S	L	F	D	H	I	L	X	K	H		Unknown	a
	K	L	F	K	V	V	X	N	Y			Unknown	a
	K	L	Y	E	K	V	Y	T	Y	K		Unknown	a
	K	L	F	N	I	M	V	T	Y			Unknown	a
	K	L	F	E	K	V	Y	N	Y			Unknown	a
	K	L	F	K	V	T	F	S	Y			Unknown	a
	G	L	F	P	X	Q	F	A	Y			Unknown	a
	S	L	F	E	L	V	F	X	Y			Unknown	a
	S	L	X	E	K	T	F	D	Y			Unknown	a
	S	L	H	K	Y	X	f	e	Y			Unknown	a
	K	M	F	N	I	T	v	T	Y			Unknown	a
	K	L	F	V	K	V	y	N	Y			Unknown	a
	K	I	V	R	K	P	G	M	A			Unknown	a
T-cell epitopes	R	L	R	D	L	L	L	I	V	T	R	HIV-1 env gp41 768–778	c
	Q	V	P	L	R	P	M	T	Y	K		HIV-1 nef 73–82	d
	T	V	Y	Y	G	V	P	V	W	K		HIV-1 env gp120 36–45	e
	R	L	R	P	G	G	K	K	K			HIV-1 gag p17 20–29	e
	I	L	R	G	S	V	A	H	K			Influenza NP 265–273	f

References:
a: DiBrino et al. 1993a; b: Maier et al. 1994; c: Takahashi et al. 1991; d: Koenig et al. 1990; e: Venet and Walker 1993; f: DiBrino et al. 1993b; g: Kubo et al. 1994

Table 2 (Continued)
E HLA-A*1101

	Position 1	2	3	4	5	6	7	8	9	10	11		Source	Ref.
Anchor or auxiliary anchor residues		V	M				L		K	K	K			a, b, c
		I	L				I							
		F	F				Y							
		Y	Y				V							
			I				F							
			A											
Other preferred residues	A	T	N	P	P	I		R	R	R	R			
			D	G	I	V		K	D					
			E	D	F	M		N						
			Q	E	V			E						
				K	M			Q						
Examples for ligands	A	V	M	K	P	E	A	E	K	R	K		Unknown	b
	A	V	I	L	P	P	L	S	P	Y	F	K	HSB 66 EST 18–29	b
	A	S	F	D	K	A	K	L	K	K			Thymosin β-10 11–20	b
	G	Q	Y	G	N	P	L	N	K				Cattle metalloproteinase 19–27	b
	G	V	M	P	S	H	F	S	R				Ribosomal protein S19 93–101	b
	Y	F	D	P	A	N	G	K	F	S	K		Elongation factor 2 265–275	b
	A	T	A	G	D	G	L	I	E	L	R	K	Prohibitin (rat) 229–240	b, c
	S	T	Y	Y	G	S	F	V	T	R			Unknown (also presented by A33)	a, b
	S	V	L	N	L	V	I	V	K				Ribosomal protein S6 107–115	c
	K	V	V	N	P	L	F	E	K				Ribosomal protein L7A 25–33	c
	R	T	Q	N	V	L	G	E	K				Ribosomal protein S3 54–62	c
	G	T	M	T	T	S	X	Y	K				Unknown	c
	A	S	F	D	K	A	K	L	K				Thymosin β-10 11–19	c
	A	A	M	X	D	T	V	V	F	K			Unknown	c
	R	V	E	Q	A	V	E	S	M	V	K		Unknown	c
T-cell epitope	I	V	T	D	F	S	V	I	K				EBNA 4 416–424	a, d

References:
a: Zhang et al. 1993; b: Falk et al. 1994c; c: Kubo et al. 1994; d: Gavioli et al. 1993

F HLA-A24

	Position 1	2	3	4	5	6	7	8	9	Source	Ref.
Anchor or auxiliary anchor residues		Y			I	F			I		a
					V				L		
									F		
Other preferred residues			N	D			Q	E			
			E	P			N	K			
			L								
			M								
			P								
			G								
Examples for ligands	K	Y	P	E	N	F	F	L	L	Protein phosphatase 1 113–121	b
	Y	Y	E	E	Q	H	P	E	L	NK/T-cell activation protein 107–115	b
	A	Y	V	H	M	V	T	H	F	Unknown	b
	V	Y	X	K	H	P	V	S	X	Unknown	b
T-cell epitope	R	Y	L	K	D	Q	Q	L	L	HIV gp 41 583–591	c

References:
a: Maier et al. 1994; b: Kubo et al. 1994; c: Dai et al. 1992

Table 2 (Continued)

G HLA-A*3101

	Position											Comments	Ref.
	1	2	3	4	5	6	7	8	9				
Anchor or auxiliary anchor residues		L V Y F	F L Y W			L F V I			R				a
Other preferred residues	K R	T Q	K N	P D E G S V T	P I V F L Y W	T N D E R	N V R F T H L Y	L R N Q				P1 deduced from individual ligands	
												Source	
Examples for ligands	L	Q	F	P	V	G	R	V	H	R		Histon H2 a 23–32	a
	Q	Q	L	Y	W	S	H	P	R			Ribosomal protein S29 (rat) 3–11	a
	R	G	Y	R	P	R	F	R	R			CCAAT-binding transcription factor 240–248	a
	K	V	F	G	P	I	H	E	R			[GlcNac]-P-transferase 371–379	a
	K	I	M	K	W	N	Y	E	R			Unknown	a
	R	Y	M	D	A	W	N	T	Y	S	R	Lamin B2	a
T-cell epitope	S	T	L	P	E	T	T	V	V	R	R	Hepatitis B cAg 141–151	b

References:
a: Falk et al. 1994c; b: Missale et al. 1993

H HLA-A*3302

	Position												Comments	Ref.
	1	2	3	4	5	6	7	8	9					
Anchor or auxiliary anchor residues		A I L F Y V							R					a
Preferred residues	D E	T	L K	P	P	I L F							P1 deduced from individual ligands	
Other possible residues	M		Q W E N	R D E G S H P	R I F P V L W	R D H Y	H Y V T S	Q N E M						
													Source	
Examples for ligands	D	M	A	A	Q	I	T	Q	R				HLA class I α-chain 161–169	a
	E	S	G	P	S	I	V	H	R				Actin 364–372	a
	T	Y	Y	G	S	F	V	T	R				Unknown	a
	D	Y	I	H	I	R	I	Q	Q	R			Human cDNA HSB15F102 65–74	a
	E	I	M	K	W	N	R	E	R				Unknown	a
	T	I	M	P	K	D	I	Q	L	A	R	R	Histon 3.1/3.3 118–129	a
T-cell epitope	I	V	G	L	N	K	I	V	R				HIV p24 gag 267–275	b, c

References:
a: Falk et al. 1994c; b: Buseyne et al. 1993; c: Buseyne and Riviere 1993

Table 2 (Continued)
I HLA-A68.1

	Position 1	2	3	4	5	6	7	8	9			Source	Ref.
Anchor residues		V							R				a
		T							K				
Examples for ligands	A	V	A	A	V	A	A	R	R			Unknown	a
	E	V	A	P	P	E	Y	H	R			Unknown	a
	E	V	A	P	P	E	Y	H	R	K		Unknown	a
	D	V	F	R	D	P	A	L	K			Homologous ribosomal 60S	a
	K	T	G	G	P	I	Y	K	R+			Influenza NP 91–99	a, b
	E	V	I	L	I	D	P	F	H	K		Unknown	a
	T	V	F	D	A	K	R	L	I	G	R	HSP 70B / HSC70 66–76	a
	X	V	L	K	X	I	A	K	R*			Unknown	d
	P	V	K	Q	V	V	Y	H	R*			Unknown	d
	E	S	G	P	S	I	V	H	R	K*		β-Actin 364–373	d
	T	T	X	T	T	T	N	A	R*			Unknown	d
	D	T	T	P	T	X	X	R*				Unknown	d
T-cell epitopes	S	T	L	P	E	T	T	V	V	R	R	Hepatitis B cAg 141–151	c

* Class I ligands allocated to A68.1 by motif +Also a T-cell epitope

References:
a: Guo et al. 1992; b: Silver et al. 1992; c: Missale et al. 1993; d: Harris et al. 1993

Table 3 HLA-B motifs
A HLA-B7

	Position 1	2	3	4	5	6	7	8	9			Source	Ref.
Anchor or auxiliary anchor residues		P	R						L				a, b
									F				
Other preferred residues				D	D	F	L						
				G	P	T							
Also detected	A		D	E	I	R	V						
	H		E	H	V	L							
	S		Q	L		I							
			K	K									
			Y	S									
			F	T									
			M	P									
			N										
			A										
Examples for ligands	A	P	R	T	V	A	L	T	A			HLA-DP signal sequence 9–17	a
	A	P	R	T	V	A	L	T	A	L		HLA-DP signal sequence 9–18	a
	A	P	R	A	X	X	X	X	X			Unknown	a
	A	P	R	X	P	X	T	G	X			Unknown	a
	A	P	R	A	S	R	P	S	X			Unknown	a
	A	P	R	T	L	V	L	L	L			HLA-A2.1 signal sequence 5–13	a
	M	P	R	G	V	V	V	T	X			Unknown	a
	S	P	R	Y	I	F	T	M	L			Topoisomerase II 801–809	a
	A	P	A	P	T	V	A	V	X			Unknown	a
	R	P	S	G	P	G	P	E	X			Unknown	a
	L	V	M	A	P	R	T	V	L			HLA-B7 signal sequence 2–10	a
	R	V	M	A	P	R	A	X	X			Unknown	a
	A	P	R	A	F	X	P	X	P	V		Unknown	a
	A	A	S	K	E	R	S	G	V	S	L	Histone H1 49–59	a
	A	P	R	S	N	G	M	V	X			Unknown	c
	A	P	R	Q	P	G	X	M	A			Unknown	c
	A	P	A	P	P	P	K	p	M			Ribosomal S26 protein 107–115	c
	A	P	Y	G	G	P	X	A	X			Unknown	c
T-cell epitope	T	P	G	P	G	V	R	Y	P	L		HIV-1 nef 128–137	d

References:
a: Huczko et al. 1993; b: Maier et al. 1994; c: Engelhard 1994; d: Culmann et al. 1991

Table 3 (Continued)
B HLA-B8

	Position 1	2	3	4	5	6	7	8	9	Source	Ref.
Anchor residues			K		K				L		a, b, d
					R						
Other preferred residues	G		R	E		N	E	E	F		
	L			Q		Q	H	Q	M		
	I			D		H	M	H			
				H		I	N	S			
				L		L	D	L			
				S		Y	Q	V			
				T		V	S	D			
				R		E	T	T			
				G		M	Y				
				K		S					
						T					
						F					
Examples for ligands	H	P	K	Y	K	T	E	L		Tristetraproline 148–155	d
	I	L	K	Q	K	I	A	d	I	IL-6 precursor 161–169	d
	E	L	K	V	K	N	I	e	I	Restin 1273–1281	d
	E	P	K	Y	K	T	Q	L		Yeast PRAI-SCS 95–102	d
	V	P	K	L	K	V	X	A	L	Rat ribosomal prot. L18, 94–102	d
	F	A	K	P	R	V	G	G		Unknown	d
	S	P	K	L	K	Y	M	Q		Unknown	d
	E	L	K	K	K	T	N	I		Unknown	d
	S	P	K	E	K	I	X	Y		Unknown	d
	X	A	K	E	K	L	A	D		Unknown	d
	S	P	K	E	K	Y	E	X		Unknown	d
	E	L	K	E	K	T	Q	L		Unknown	d
	L	P	K	V	K	L	A	L		Unknown	d
	H	p	K	Y	K	T	E	L		Unknown	d
	V	L	D	L	K	I	V	A	F	Unknown	d
	G	P	K	E	K	X	A	M		Unknown	d
	G	L	K	V	K	G	N	E	F	Unknown	d
	F	L	K	P	K	F	V	A	L	Unknown	d
	E	L	K	I	K	V	Y	X	I	Unknown	d
	S	L	K	E	K	V	X	L		Unknown	d
	E	L	K	E	K	X	y	e	I	Unknown	d
	I	P	K	L	K	N	V	K	r	Unknown	d
	S	L	K	I	K	X	L			Unknown	d
	D	L	K	Q	K	N	E	L		Unknown	d
T-cell epitopes	E	L	R	S	R	Y	W	A	I	Influenza NP 380–388	b
	F	L	R	G	R	A	Y	G	L	EBNA 3 339–347	c
	E	I	Y	K	R	W	I	I	L	HIV gag p24, 262–270	d, e
	G	E	I	Y	K	R	W	I	I	HIV gag p24, 261–269	d, e
	E	I	K	D	T	K	E	A	L	HIV gag p17, 93–101	d, f

References:
a: Malcherek et al. 1993; b: Sutton et al. 1993; c: Burrows et al. 1990; d: DiBrino et al. 1994; e: Phillips et al. 1989; f: Achour et al. 1990

Table 3 (Continued)
C HLA-B*2702

	Position										Source	Ref.
	1	2	3	4	5	6	7	8	9			
Anchor residues		**R**							**F** **Y** **I** **L** **W**			a
Other preferred residues	K		F L X	G P K D E Q T S	I K E V M T	I V Y R D H E Q	Y L V T F	K V D E R				
Examples for ligands	S	**R**	D	K	T	I	I	M	**W**		HGNBPβ-subunit 35–43	a
	G	**R**	L	T	K	H	T	K	**F**		Rat ribosomal protein L36 36–44	a
	R	**R**	F	V	N	V	V	P	T	**F**	Human fau protein 114–123	a
	K	**R**	Y	K	S	I	V	K	**Y**		HFPS 191–199	a
	K	**R**	K	K	A	Y	A	D	**F**		Cytochrome C oxidase 42–50	a
	K	**R**	G	I	L	T	L	K	**Y**		Actin 63–71	a
	G	**R**	F	G	V	G	N	R	**Y**		Unknown	a
	G	**R**	F	K	L	I	V	L	**Y**		Unknown	a

References:
a: Rötzschke et al. 1994

Table 3 (Continued)
D HLA-B*2705

	Position												Source	Ref.
	1	2	3	4	5	6	7	8	9					
Anchor residues		R							L F					a, b
Other preferred residues	A G K R		L I F	K Q E G	I V L P G	I A N Q D V K	I T Y M L W N V P	K N R E Q	Y M I R H K					
Examples for ligands	G	R	L	T	K	H	T	K	F				Rat ribosomal protein L 36 36–44	b
	A	R	L	F	G	I	R	A	K				HBBCP 190–198	a, b
	R	R	L	G	X	Q	Y	R	R				Unknown	b
	R	R	F	G	D	K	L	N	F				Immediate early response gene 87–95	b
	G	R	v	F	I	I	K	E					Homologous to Il-1 receptor antagonist	b
	G	R	X	X	i	f	X	r	f	G	Y	H	Unknown	b
	T	R	Y	P	I	L	A	G	H				Cytochrome P450 20–28	b
	r	r	i	s	g	V	D	R	Y				Unknown	a, b
	K	R	F	S	F	K	K	S	F				Cattle MARCKS 155–163	b
	A	R	L	Q	T	A	L	L					Rat core histone 188–196	b
	R	R	X	P	I	F	S	R	L				TIS 11B protein 325–333 (X = L)	b
	R	R	F	M	q	Y	Y	V	Y				Homologous to proteasome subunit C5 127–135	b
	R	R	I	K	E	I	V	K	K	H			HSP 86 200–209	b
	R	R	M	G	P	P	V	G	G	H	R		Ribonucleoprotein L 312–322	b
	R	R	I	K	E	I	V	K	K				HSP 89 a 200–208	a
	G	R	I	D	K	P	I	L	K				Ribosomal protein L8 173–181	a
	R	R	S	K	E	I	T	V	R				ATP-dependent RNA helicase 77–85	a
	K	R	F	E	G	L	T	Q	R				Unknown	a
	R	R	V	K	E	V	V	K	k				HSP 89 B 195–203	a
	F	R	Y	N	G	L	I	H	R				60 S ribosomal protein L28 37–45	a
	R	R	Y	Q	K	S	T	E	L				Histon H3.3 52–60	a
	R	R	W	L	P	A	G	d	a				Elongation factor 2 341–349	a
	R	R	I	S	G	V	D	R	Y				Unknown	a
	R	R	F	T	R	P	E	H					Unknown	a
	K	K	Y	Q	K	S	T	E	L				Unknown	c
	XXLNSQDQQCDSSLVE												Draft-1 protooncogene 1–16	i
B*270x-restricted T-cell epitopes	S	R	Y	W	A	I	R	T	R				Influenza NP 383–391	d
	R	R	R	W	R	R	L	T	V[x]				EBNA LMP2 236–244	e
	R	R	Y	P	D	A	V	Y	L				Measles F protein 438–446	f
	R	R	I	Y	D	L	I	E	L				EBNA 3C 258–266	e
	K	R	W	I	I	L	G	L	N	K			HIV-1 gag p24 265–274	d, g
	G	R	A	F	V	T	I	G	K				HIV-1 gp120 314–322	d
	R	R	K	A	M	F	E	D	I				HSP 60 284–292	h

[x] B*2704-restricted

References:
a: Jardetzky et al. 1991; b: Rötzschke et al. 1994; c: Shepherd et al. 1993; d: Huet et al. 1990; e: Brooks et al. 1993; f: van Binnendijk et al. 1993; g: Buseyne et al. 1993; h: Cerrone et al. 1991; i: Frumento et al. 1993

Table 3 (Continued)
E HLA-B*3501

	Position										Source	Ref.
	1	2	3	4	5	6	7	8	9	10		
Anchor or auxiliary anchor residues		**P**							**Y** **F** **M** **L** **I**	**Y**		a, b
Other preferred residues	M	A V Y R D	I L F V M E T Y N	K D E G P	D I V T E G L M	I Q K V L M	V N E Q T K	E Q V T				
T-cell epitopes	K	**P**	K	D	E	L	D	**Y**			P. falciparum CSP 368–375	a
	K	S	K	D	E	L	D	**Y**			P. falciparum CSP 368–375	a
	K	**P**	N	D	K	S	L	**Y**			P. falciparum LS 1850–1857	a
	A	S	R	C	W	V	A	**M**			HCV E1 235–242	c

References:
a: Hill et al. 1992; b: Falk et al. 1993b; c: Koziel et al. 1992

F HLA-B*3701

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		**D** E			V I			**F** **M** L	**I** **L**		a
Other preferred residues	K Q	H P G S L			T R A D G H M		Q K Y L	T E N D Q G H			
T-cell epitope	E	**D**	L	R	V	L	S	**F**	**I**	Influenza NP 339–347	b

References:
a: Falk et al. 1993b; b: Townsend et al. 1986

G HLA-B*3801

	Position 1	2	3	4	5	6	7	8	9	Source	Ref.
Anchor or auxiliary anchor residues		H	D						F		a
			E						L		
Other preferred residues	I	F	I	G	M	V	Y	K	I		
		P	A	E	T	I	V	Y			
		W	S	P	V	T	N	N			
		Y	N	L	A	K		R			
			M	V	E	R		T			
			V		G	N					
					L	H					
					K						
					S						
Examples for ligands	E	H	A	G	V	I	S	V	L	Unknown	a
	T	H	D	E	L	E	D	K	L	Unknown	a
	Q	Y	D	E	A	V	A	Q	F	Histone binding protein 627–635	a
	Y	P	D	P	A	N	G	K	F	Elongation factor 2 265–273	a
	S	H	I	G	D	A	V	V		Cyclin 152–159	a
	Y	H	E	D	I	H	T	Y	L	Cyclin A 178–186	a
	T	F	D	V	A	P	S	R	L	Pm5 protein 270–278	a

References:
a: Falk et al. 1995b

H HLA-B*39011

	Position 1	2	3	4	5	6	7	8	9	Source	Ref.
Anchor or auxiliary anchor residues		R				I			L		a
		H				V					
						L					
Other preferred residues			A	D	V	N	N	S	V		
			D	E	Y		Y	K	I		
			I	G	I		F	R	M		
			L	P	L			E			
			F	K	F			T			
			V		T						
			M		G						
			S		K						
			T		N						
			Y		P						
Examples for ligands	S	H	I	G	D	A	V	V		Cyclin 152–159	a
	I	H	E	P	E	P	H	I		CKShs1 protein 59–66	a
	S	R	D	K	T	I	I	M		GBLP 35–42	a

References:
a: Falk et al. 1995b

Table 3 (Continued)

I HLA-B*3902

	Position									Ref.
	1	2	3	4	5	6	7	8	9	
Anchor or auxiliary anchor residues		K Q			I L F V				L	a
Other preferred residues	K A		A I F V N L T Y E H S	G P	N E G P Q S T	V Y T H F I M P R	V L T Y N D H	T S R	F M	

References:
a: Falk et al. 1995b

K HLA-B40*

	Position												Source	Ref.
	1	2	3	4	5	6	7	8	9	10	11			
Anchor or auxiliary anchor residues		E	F I V						L W M A					a
Examples for ligands	T	E	F	P	K	E	R	H	L	R	L		Unknown	a
	G	E	F	P	N	K	N	X	L				Unknown	a
	G	E	F	P	N	K	N	X	L	Y	A		Unknown	a
	G	E	F	P	G	K	I	F	L	Y	A		Unknown	a
	W	E	F	L	Q	P	I	L	L				Unknown	a
	G	E	F	I	P	G	N	D	L	H	R		Unknown	a
	G	E	F	P	P	X	D	N	W				Unknown	a
	E	E	F	Y	V	D	L	E	R				HLA-DQ α 33–41	a
	N	E	F	P	D	I	D	I	R				Unknown	a
	A	E	F	P	K	X	E	A	R				Unknown	a
	A	E	I	G	E	V	I	V	L	W	X	W	Unknown	a
	A	E	I	P	G	E	I	A	L				Unknown	a
	G	E	I	L	D	V	F	D	A				IRE-BP 695–703	a
	F	E	I	P	X	L	D	V	A				Unknown	a
	D	E	V	T	P	Q	P	Q	L	V			Unknown	a
	K	E	V	G	V	D	V	A	L	Y	A		Unknown	a
	K	E	S	T	L	H	L	V	L				Ubiquitin 63–71	a
	G	E	V	D	V	E	Q	H	T				Cyclin B 313–321	a
	H	E	E	T	P	P	T	T	S				c-myc 241-249	a

* Motif and ligands deduced by exclusion: Class I ligands from a c-*myc* transfected B-cell line expressing A2, A68, and B40 were sequenced. Those not containing an A2 or A68 motif were thought to contain B40 ligands.

References:
a: Harris et al. 1993

Table 3 (Continued)

L HLA-B*4402

	Position 1	2	3	4	5	6	7	8	9	10	Ref.
Anchor or auxiliary anchor residues		**E**							**F** **Y**	F Y	a
Preferred residues	A S		M I L D		I	V	Y				
Others	D		N	P R K							

References:
a: Fleischhauer et al. 1994

M HLA-B*4403

	Position 1	2	3	4	5	6	7	8	9	10	Source	Ref.
Anchor or auxiliary anchor residues		**E**							**Y** **F**	Y F		a
Preferred residues	A S		M I L V D									
Others			N	P R K	I V K		Y F					
Examples for ligands	A	E	D	K	E	N	Y	K	K	F	HSP 90 427–436	a
	A	E	M	G	K	G	S	F	K	Y	Elongation factor 2 48–57	a
B*440x-restricted T-cell epitope	E	E	N	L	L	D	F	V	R	F	EBNA 6 130–139	b

References:
a: Fleischhauer et al. 1994; b: Khanna et al. 1992

Table 3 (Continued)

N HLA-B*5101

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		A							F		a
		P							I		
		G									
Other preferred residues	I	W	I	G	V	N	K	T	W		
	L	F	L	V	T	I	Q		M		
	V		M	I	G	L	R		V		
	Y		F	K	A	K	E		L		
	D		W	E	I	Q					
			Y	D	S						
			V								
			E								
			H								
			D								
			R								
			N								
Examples for ligands	Y	P	F	K	P	P	K	V		UBC5, yeast 61–68	a
	D	A	H	I	Y	L	N	H	I	Thymidylate synthase 253–261	a
	T	G	Y	L	N	T	V	T	V	GBLP 192–200	a
	d	A	Y	A	L	N	H	T	L	Unknown	a
	I	P	P	E	V	N	R	Q	L	Unknown	a

References:
a: Falk et al. 1995a

O HLA-B*5102

	Position										Source	Ref.
	1	2	3	4	5	6	7	8	9			
Anchor or auxiliary anchor residues		P	Y						I			a
		A							V			
		G										
Other preferred residues			F	G	V	I	R	T				
			V	E	Q	N	E	R				
			L	K	N	Q	Q	Y				
			I	L	G	T	K					
				T	T							
				Q								
				R								
				N								
				H								
Examples for ligands	Y	A	Y	D	G	K	D	Y	I		MHC I α chain 140–148	a
	Y	P	F	K	P	P	K	V			UBC5, yeast 61–68	a
	L	P	P	G	R	I	I	K	X		Unknown	a
	L	P	F	T	V	I	L	v			CDC25 homol. 560–567	a
	T	G	Y	L	N	T	V	T	V		GBLP 192–200	a
	F	A	Y	D	G	K	D	Y	I		MHC I α chain 140–148	a
	F	P	S	E	I	V	G	K	R	I	Ribosomal protein S7/S8A 135–144	a
	M	P	W	F	K	G	w	K	V		Elongation factor 1a 208–216	a

References:
a: Falk et al. 1995a

Table 3 (Continued)
P HLA-B*5103

	Position									Comments	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		A P G	Y						V I F	Anchor at 9 deduced from individual ligands	a
Other preferred residues	T V D	F W	F D L	E L N R G Q T V	G A V N Q M R	I K T	V M				
										Source	
Examples for ligands	T	G	Y	L	N	T	V	T	V	GBLP 192–199	a
	D	A	H	I	Y	L	N	H	I	Thymidilate synthase 253–261	a
	Y	F	D	d	t	L	E	D	F	Unknown	a

References:
a: Falk et al. 1995a

Q HLA-B*5201

	Position									Comments	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Q	F Y W		L I V			I V	I V	C-terminal anchor at 8 or 9	a
Other preferred residues	V L I	M F P	I L P D K	L I V P K E A	M F A T G	K N L T S	K E Q Y	M F	M F		
										Source	
Examples for ligands	T	G	Y	L	N	T	V	T	V	GBLP 192–200	a
	G	Q	F	K	T	Y	A	I		Ribos. prot. S21 60–67	a
	H	S	T	I	M	P	R	L		P1-CDC21 259–266	a
	G	F	Y	P	G	S	I	E	V	MHC II β chain 150–158	a
	V	Q	I	F	G	N	K	M		RBAP-2 266–273	a
	Y	P	D	P	A	N	G	K	F	Elongation factor 2 265–273	a
	L	Q	F	P	V	G	R	I		Histone 2a Z 25–32	a
	H	M	Y	I	F	L	H	T	V	Unknown	a

References:
a: Falk et al. 1995a

Table 3 (Continued)
R HLA-B53

	Position 1	2	3	4	5	6	7	8	9	Source	Ref.
Anchor residues		**P**									a
T-cell epitope	K	**P**	I	V	Q	Y	D	N	F	P. falciparum LSA-1 1786–1794	a

References:
a: Hill et al. 1992

S HLA-B*5801

	Position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor or auxiliary anchor residues		**A** S **T**		P E **K**	V I L M F				**F** **W**			a
Other preferred residues	K R I	G	G T I L V F Y N Q	D Q R	A D N T Y W Q	I V L F	L Y M N	N R K T	Y			
Examples for ligands	K	A	G	Q	V	V	T	I	W		Lamin C 490–498	a
	A	G	D	R	T	F	Q	K	W		MHC class I 260–268	a
	I	t	T	K	A	I	S	R	F		Unknown	a
	R	T	D	G	K	V	F	Q	F		Ribosomal protein L30 23–31	a
	I	T	S	Q	D	V	L	H	S	W	Cytochrome C oxidase 154–163	a
	I	S	D	S	N	P	F	L	T	Q	Unknown	a
	K	t	D	e	V	V	T	L	F		Unknown	a
	V	T	S	P	L	T	V	E	W		MHC class II β 209–217	a
	g	A	V	N	V	V	M	T	f		Glucose transporter 5 322–330	a

References:
a: Falk et al. 1995c

Table 3 (Continued)

T HLA-B60 (B*40012)

	Position 1	2	3	4	5	6	7	8	9			Source	Ref.
Anchor or auxiliary anchor residues		E					I V		L				a
Other preferred residues			A V I L M F S D N	P K D G N Q T	L I V D T N P G K Q	K N P V I D R Q	L Y M	K R Q					
Examples for ligands	K	E	S	T	L	H	L	V	L			Ubiquitin 63–71	a
	H	E	A	T	L	R	c	w	A	L		MHC class I 221–230	a
	Y	E	I	H	D	G	M	N	L			HSHMO2C05	a
	S	E	S	P	I	V	V	V	L			Signal peptidase 45–54	a
	I	E	V	D	P	D	T	K	E	m	L	Ribosomal protein S17 95–105	a

References:
a: Falk et al. 1995c

U HLA-B61 (B*4006)

	Position 1	2	3	4	5	6	7	8	9	Comments / Source	Ref.
Anchor or auxiliary anchor residues		E	F I L V Y W			I			V		a
Other preferred residues	G R	P	M T	E G P S N D K A R N Q	V I L M D G V F N S K	N	Y V L W I T R D Q G	K S	A P	P1 deduced from individual ligands	
Examples for ligands	G	E	F	G	G	F	G	S	V	IEF (mRNA) 9306 127–135	a
	E	E	F	Q	F	I	K	K	A	Associated-microfibril. protein 72–80	a
	G	E	F	V	D	L	Y	V		Ribosomal protein S21 6–13	a
	R	E	R	R	D	N	Y	V		Ribosomal protein S17 77–84	a
	R	E	I	I	I	N	A	V		Ribonucl. reductase 290–297	a
	G	E	F	S	I	T	Y	K		Ribosomal protein S15 116–123	a
	G	E	H	G	L	i	I	R	V	Unknown	a
	R	E	M	I	P	F	A	D	i	Unknown	a

References:
a: Falk et al. 1995c

Table 3 (Continued)
V HLA-B62 (B*1501)

	Position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor or auxiliary anchor residues		Q L			I V				F Y			a
Other preferred residues	I	M V	K A N F P Y H R	P E G D	G L F T	V T G I	V T L I	Y V T				
Examples for ligands	V	L	K	P	G	M	V	V	T	F	Elongation factor 1 α 271–280	a
	Y	L	G	E	F	S	I	T	Y		Ribosomal protein S15 114–122	a
	G	Q	R	K	G	A	G	S	V		Ribosomal protein L8 (rat) 7–15	a
	K	I	K	S	F	V	K	V	Y		Ribosomal protein L27 66–74	a
	I	Q	P	G	R	G	F	V	L	Y	Unknown	a
	S	Q	F	G	G	G	S	Q	Y		Unknown	a
	G	Q	R	K	P	A	T	S	Y		Ribosomal protein L28 (rat) 68–76	a
	V	Q	G	P	V	G	L				Collagen α1 1106–1112	a
T-cell epitopes	I	L	G	N	K	I	V	R	M	Y	HIV gag 267–276	b

References:
a: Falk et al. 1995c; b: Buseyne et al. 1993

W HLA-B*7801

	Position 1	2	3	4	5	6	7	8	Comments	Ref.
Anchor or auxiliary anchor residues		P A G				I L F V		A	This motif is only partial; the C-terminal anchor has not been determined	a
Other preferred residues			Y D W	F D G L V S Q R N	D G V N R Q S T		A V N K Q E	K S		

References:
a: Falk et al. 1995a

Table 4 HLA-C motifs
A HLA-Cw*0301

	Position												Source	Ref.
	1	2	3	4	5	6	7	8	9					
Anchor or auxiliary anchor residues			V I Y L M	P		F Y			L F M I					a
Other preferred residues		A R	E N	E R	N	M	Q K S M	T						
T-cell epitopes	H	Q	A	I	S	P	R	T	L				HIV gag 144–152	b
or	Q	M	V	H	Q	A	I	S	P	R	T	L	HIV gag 141–152	

References:
a: Falk et al. 1993a; b: Littaua et al. 1991

B HLA-Cw*0401

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Y P F				V I L			L F M		a
Other preferred residues			D H	D E P	A H M T R		A	K S H			
T-cell epitope	S	F	N	C	G	G	E	F	F	HIV-1 gp 120 380–388	b

References:
a: Falk et al. 1993a; b: Johnson et al. 1993

C HLA-Cw*0602

	Position											Source	Ref.
	1	2	3	4	5	6	7	8	9				
Anchor or auxiliary anchor residues					I L F M	V I L			L I V Y				a
Other preferred residues	I F K Y	P R	P I G F Y K N A	P E D Q L	K	A T S	R K Q N	Y E Q N R G T S K					
Examples for ligands	Y	Q	F	T	G	I	K	K	Y			Unknown	a
	V	R	H	D	G	G	N	V	L			Unknown	a
	F	A	F	p	I	I	q	R	V			Unknown	a
	X	Q	r	T	P	k	A	g	I	Y	Y	Unknown	a

References:
a: Falk et al. 1993a

Table 4 (Continued)
D HLA-Cw*0702

	Position												Source	Ref.
	1	2	3	4	5	6	7	8	9					
Anchor or auxiliary anchor residues		Y			V	V			Y					a
		P			Y	I			F					
					I	L			L					
					L	M								
					F									
					M									
Other preferred residues		R	P	D	T	A	Y	E						
		D	G	E		R	M	A						
			A	V			N	F						
				Q			R	D						
				P			V	K						
				S			F							
				G			E							
Examples for ligands	K	Y	F	D	E	H	Y	E	Y				CKS-2 11–19	a
	R	Y	R	P	G	T	V	A	L				Histone H3.3 40–48	a
	N	K	A	D	V	I	L	K	Y				Protein synthesis factor eIF-4C 87–95	a
	I	Y	P	q	n	v	i	L	Y				Unknown	a
	I	R	K	P	Y	I	w	E	Y				Glutamyl-tRNA synthetase 343–351	a
	N	Y	G	G	G	N	Y	G	S	G	S	Y	Homologous hnRNP A2 or B1 (S11 = N) 277–288	a
	F	Y	P	P	y	l	Y						Unknown	a
	X	M	P	P	f	L	d	G					Unknown	a

References:
a: Falk et al. 1993a

Table 5 Processing motif for all MHC class II ligands

Absolute position																	Ref.
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
	P										p	p	p	p	p		a, b, c

References:
a: Falk et al. 1994b; b: Kropshofer et al. 1993; c: Malcherek et al. 1993

Table 6 Human MHC class II motifs
A HLA-DRB1*0101

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor residues		Y,V,			L,A		A,G			L,A			a, b, e
		L,F,			I,V		S,T			I,V			
		I,A			M,N		P			N,F			
		M,W			Q					Y			
Examples for ligands	VGSD	W	R	F	L	R	G	Y	H	Q	YA	HLA-A2 103–117	c
	VGSD	W	R	F	L	R	G	Y	H	Q	YAYDG	HLA-A2 103–120	c
	VGSD	W	R	F	L	R	G	Y	H	Q	Y	HLA-A2 103–116	c
	GSD	W	R	F	L	R	G	Y	H	Q	YA	HLA-A2 104–117	c
	LPKPPKPVSK	M	R	M	A	T	P	L	L	M	QALPM	Invariant chain 97–120	c
	IPAD	L	R	I	I	S	A	N	G	C	K	Na+-K+-ATPase 199–216	c
	RVE	Y	H	F	L	S	P	Y	V	S	PKESP	Transferrin receptor 680–696	c
	YKHT	L	N	Q	I	D	S	V	K	V	WPRRPT	Cattle fetuin 56–74	c
	AILE	F	R	A	M	A	Q	F	S	R	KTD	Unknown	d
	PK	Y	V	K	Q	N	T	L	K	L	AT*	Influenza HA 306–318	e

* Alignment determined by structural analysis
References:
a: Hammer et al. 1992; b: Falk et al. 1994b; c: Chicz et al. 1992; d: Kropshofer et al. 1992; e: Stern et al. 1994

Table 6 (Continued)
B HLA-DRB1*0301 (DR17)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or auxiliary anchor residues		**L,I F,M V**			**D**		K,R E,Q N			Y,L F			a, b, c
Examples for ligands	ISNQ	**L**	T	L	**D**	S	N	T	K	**Y**	FHKLN	Apolipoprotein B 2877-2894	a
	ISNQ	**L**	T	L	**D**	S	N	T	K	**Y**	FHKL	Apolipoprotein B 2877-2893	a
	ISNQ	**L**	T	L	**D**	S	N	T	K	**Y**	FHK	Apolipoprotein B 2877-2892	a
	VDT	**F**	L	E	**D**	V	**K**	N	L	**Y**	HSEA	α1-Antitrypsin 149-164	a
	KPRA	**I**	V	V	**D**	P	V	H	G	**F**	MY	LDL-Receptor 518-532	a
	KQT	**I**	S	P	**D**	Y	**R**	N	M	I		IgG2a, Membrane domain	a
	YPD	**F**	I	M	**D**	P	**K**	E	K	D	KV	Unknown	a
	NIQ	**L**	I	N	**D**	Q	**E**	V	A	R	FD	Unknown	a
	LLS	**F**	V	R	**D**	L	**N**	Q	Y	R	ADI	Transferrin receptor 618-632	a
	LPKPPKPVSK	**M**	R	M	A	T	P	L				Invariant chain 97-113	d, e, f
	LPKPPKPVSK	**M**	R	M	A	T	P	L	L	M	QALP	Invariant chain 97-119	d, e, f
	LPKPPKPVSK	**M**	R	M	A	T	P	L	L	M	QALPM	Invariant chain 97-120	d, e, f
	PKPPKPVSK	**M**	R	M	A	T	P	L				Invariant chain 98-113	d, e, f
	PKPPKPVSK	**M**	R	M	A	T	P	L	L	M	QA	Invariant chain 98-117	d, e, f
	KPPKPVSK	**M**	R	M	A	T	P	L	L	M	Q	Invariant chain 99-116	d, e, f
	KPPKPVSK	**M**	R	M	A	T	P	L	L	M	QALPM	Invariant chain 99-119	d, e, f
	VDDTQF	**V**	R	F	**D**	S	D	A	A	S	Q	HLA-A30 28-?	e
	ATKYGN	**M**	T	E	**D**	H	V	M	H	**L**	LQNA	Invariant chain 131-149	e
	VFLL	**L**	L	A	**D**	K	V	P	E	T	SLS	ACh receptor 289-304	e
	LNK	**I**	L	L	**D**	E	**Q**	A	Q	W	K	ICAM-2 64-76	e
	GPPKLD	**I**	R	K	**E**	E	**K**	Q	I	M	IDIFH	IFN-γ receptor 128-147	e
	GPPKLD	**I**	R	K	**E**	E	**K**	Q	I	M	IDIFHP	IFN-γ receptor 128-148	e
	GKFA	**I**	R	P	**D**	K	**K**	S	N	P	IIRTV	Cyt-b5 155-172	e
	YAN	**I**	L	L	**D**	R	**R**	V	P	Q	TDMTF	Apolipoprotein B 1207-1224	e
	NLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TLNKNSLK	Apolipoprotein B 1276-1295	e
	IPDNLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TLNKN	Apolipoprotein B 1273-1292	e
	IPDNLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TLNK	Apolipoprotein B 1273-1291	e
	IPDNLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TLN	Apolipoprotein B 1273-1290	a, e
	IPDNLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TL	Apolipoprotein B 1273-1289	e
	NLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TLNK	Apolipoprotein B 1276-1291	e
	NLF	**L**	K	S	**D**	G	**R**	I	K	**Y**	TLN	Apolipoprotein B 1276-1290	e
	VTT	**L**	N	S	**D**	L	**K**	Y	N	A	LDLTN	Apolipoprotein B 1294-1810	e
		V	G	S	**D**	W	**R**	F	L	R	GYHQYA	HLA-A2 103-117	e

References:
a: Malcherek et al. 1993; b: Geluk et al. 1994; c: Geluk et al. 1992; d: Riberdy et al. 1992; e: Chicz et al. 1993; f: Sette et al. 1992

Table 6 (Continued)
C HLA-DRB1*0401 (DR4Dw4)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		F,Y W,I L,V M			F,W I,L V,A D,E no R,K		N,S T,Q H,R	pol.* chg.* ali.*		pol.* ali.* K			a, b, c, d
Examples for ligands		F	V	R	F	D	S	D	A	A	SQRMEP	HLA-A2 33–47	a
	VDDTQ	F	V	R	F	D	S	D	A	A	SQRM	HLA-A2 28–45	a
		F	V	R	F	D	S	D	A	A	SQRM	HLA-A2 33–45	a
	VDDTQ	F	V	R	F	D	S	D	A	A	SPRGEP...	HLA-C 28–?	a
	DGKD	Y	I	A	L	N	E	D	L	S	S	HLA-B44 143–156	a
	LSS	W	T	A	A	D	T	A	A	Q	ITQ	HLA-B44 154–168	a
	LSS	W	T	A	A	D	T	A	A	Q	IT	HLA-B44 154–167	a
	IY	F	R	N	Q	K	G	S	H	S	GLQPTGFL	HLA-DR4β 252–270	a
	DVA	F	V	K	D	Q	T	V	I	Q	NTD	Cattle transferin 68–82	a
	YDHN	F	V	K	A	I	N	A	I	Q	KSW	Cathepsin C 170–185	a
	KHKV	Y	A	C	E	V	T	H	Q	G	...	Igκ chain C region 80–?	a
	HKV	Y	A	C	E	V	T	H	Q	G	L...	Igκ chain C region 81–?	a
	DGP	F	R	I	I	T	V	P	A	A	LDY	Unknown	a
	TGN	Y	R	I	E	S	V	L	S	S		Sphingolipid activator protein 3 165–176	a
	GERA	M	T	K	D	N	N	L	L	G	...	HSC 70 445–?	a
	XXX	Y	E	X	A	L	S	L	P	S	K...	Unknown	a
	GSLF	V	Y	N	I	T	T	N	K	Y	KAFLKQ	VLA-4 229–247	e
	SPEDF	V	Y	Q	F	K	G	M	C	Y	F	HLA-DQβ 3.2 chain 24–38	e
	AAPYEKEVP	L	S	A	L	T	N	I	L	S	AQL	PAI-1 261–281	e
	GVYF	Y	L	Q	W	G	R	S	T	L	VSVS	Ig heavy chain 121–?	e
	AEALERM	F	L	S	F	P	T	T	K	T		Cattle hemoglobin 26–41	e
	LRS	W	T	A	A	D	T	A	A	Q	ITQRKWEAA	HLA-Cw9 130–150	e
	DLSS	W	T	A	A	D	T	A	A	Q	ITQRKWEAA	HLA-Bw62 129–150	e
	APSP	L	P	E	T	T	E	N	V	V	CALG	HLA-DRα chain 182–198	e

* pol.: Polar; chg.: charged; ali.: aliphatic
References:
a: Friede and co-workers, submitted; b: Sette et al. 1993; c: Hammer et al. 1993; d: Hill et al. 1994; e: Chicz et al. 1993

D HLA-DRB1*0402 (DR4Dw10)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		V,I L,M			Y,F W,I L,M R,N no D,E		N,Q S,T K	R,K H,N Q,P; rare D,E		pol.* ali.* H			a
Examples for ligands	GPDGR	L	L	R	G	H	N	Q	F	A	YDGKD	HLA-B38 128–146	a
	GR	L	L	R	G	H	N	Q	F	A	YDGK	HLA-B38 131–145	a
	I	I	K	G	V	R	K	S	N	A	AERRG	HLA-DRα 238–252	a
		I	Y	F	R	N	Q	K	G	H	SGLQPTGFLS	DR4β 248–266	a
				F	R	N	Q	K	G	H	SGLQP	DR4β 250–261	a
	F	I	Y	F	R	N	Q	K	G	H	SGLQPTGFLS	DR4β 249–266	a
		Y	V	R	F	D	S	D	V	G	EY	DR4Dw10β 37–47	a
	LPKPPKPVSK	M	R	M	A	T	P	L	L	Q		Invariant chain 97–?	a
	FDQK	I	V	E	W	D	S	R	K	S	KYFE	BLAST-1 62–78	a
	DQK	I	V	E	W	D	S	R	K	S	KYF	BLAST-1 63–77	a
	IKI	I	S	K	I	E	N	H	E	G	VRR	Pyruvate kinase 264–278	a
	IKI	I	S	K	I	E	N	H	E	G	VR	Pyruvate-kinase 264–277	a
	FGR	I	G	R	L	V	T	R	A	A	FNSG	GAPDH 11–25	a
	FGR	I	G	R	L	V	T	R	A	A	FN	GAPDH 11–23	a
	GFGR	I	G	R	L	V	T	R	A	A	FNSG	GAPDH 10–25	a
	CNE	I	I	N	W	L	D	K	N	Q		HSC 70 574–585	a
	QPD	L	R	Y	L	F	L	N	G	N		Leucine-rich α2-glycoprotein 200–211	a

References:
a: Friede and co-workers, submitted

Table 6 (Continued)
E HLA-DRB1*0404 (DR4Dw14)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		V,I L,M			F,Y W,I L,V M,A D,E no R,K		N,T S,Q R	pol.* chg.* ali.*		pol.* ali.* K			a
Examples for ligands	GSHS	M	R	Y	F	H	T	A	M	S	RPGRGE	HLA-B60 1-?	a
	SHS	M	R	Y	F	H	T	A	M	S	RPGRGE	HLA-B60 2-?	a
	YDNS	L	K	I	I	S	N	A	S	C	TTN	GAPDH 139-154	a

* pol.: Polar; chg.: charged; ali.: aliphatic
References:
a: Friede and co-workers, submitted

F HLA-DRB1*0405 (DR4Dw15)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		F,Y W,V I,L M			V,I L,M D,E		N,S T,Q K,D	pol.* chg.* ali.*		D,E Q			a
Examples for ligands	YPTQRAR	Y	Q	W	V	R	C	N	P	D	SNS	PGSG 1-19	a
	QRAR	Y	Q	W	V	R	C	N	P	D	SNS	PGSG 4-19	a
	RAR	Y	Q	W	V	R	C	N	P	D	SNS	PGSG 5-19	a
	KPPQ	Y	I	A	V	H	V	V	P	D	Q	MIF 32-45	a
	FRE	F	K	L	S	K	V	W	R	D	QH	Transferrin receptor 173-186	a
	FRE	F	K	L	S	K	V	W	R	D	Q	Transferrin receptor 173-185	a
	RE	F	K	L	S	K	V	W	R	D	QH	Transferrin receptor 174-186	a
	RE	F	K	L	S	K	V	W	R	D	Q	Transferrin receptor 174-185	a
	VEPDH	Y	V	V	V	G	A	Q	R	D	A	Transferrin receptor 397-411	a
	EPDH	Y	V	V	V	G	A	Q	R	D	A	Transferrin receptor 398-411	a
	THY	Y	A	V	A	V	V	K	K	D	TDFK	Transferrin 92-107	a
	KELK	I	D	I	I	P	N	P	Q	E	R	Hsp 90-beta 68-81	a
	YLL	Y	Y	T	E	F	T	P	T	E	KD	β_2-microglobulin 83-96	a
	LL	Y	Y	T	E	F	T	P	T	E	KDEY	β_2-microglobulin 84-98	a
	CAIHAKR	V	T	I	M	P	K	D	I	Q	LA...	Histone H3 110-?	a
	APNT	F	K	T	L	D	S	W	R	D		ras-related protein RAB-7 (rat) 86-98	a
	VADK	I	Q	L	I	N	N	M	L	D		Phosphoglycerate kinase 216-228	a
	GSTV	F	D	N	L	P	N	P	E	I	DGDYYGW	Unknown	b
	XXXQ	Y	I	A	V	H	V	V	P	D	QT	Homol. MIF 32-46	b
	SDPIL	Y	R	P	V	A	V	A	L	D		PKM2 99-112	b
		V	P	I	Q	R	A	V	Y	Q	NVVVNNPXD	Unknown	b
	SPGTGA	Y	Y	V	L	L	N	...				Unknown	b
	KPPQ	Y	I	A	V	H	V	V	P	D	QLM	MIF 32-47	c
	KPPQ	Y	I	A	V	H	V	V	P	D	QL	MIF 32-46	c
	KPPQ	Y	I	A	V	H	V	V	P	D	Q	MIF 32-45	c
	DPIL	Y	R	P	V	A	V	A	L	D	TKGPE	PKM2 101-118	c
	DPIL	Y	R	P	V	A	V	A	L	D	TKGP	PKM2 101-117	c
	DNPQTHY	Y	A	V	A	V	V	K	K	D	TDFKL	Transferrin 88-108	c
	DNPQTHY	Y	A	V	A	V	V	K	K	D	TDFK	Transferrin 88-107	c
	NPQTHY	Y	A	V	A	V	V	K	K	D	TDFKL	Transferrin 89-108	c
	NPQTHY	Y	A	V	A	V	V	K	K	D	TDFK	Transferrin 89-107	c
	DNPQTHY	Y	A	V	A	V	V	K	K	D		Transferrin 88-103	c
	THY	Y	A	V	A	V	V	K	K	D	TDF	Transferrin 92-106	c
	LL	Y	Y	T	E	F	T	P	T	E	KDEY	β_2m 84-98	c
	L	Y	Y	T	E	F	T	P	T	E	KD	β_2m 85-26	c
	XXXXKK	V	V	V	Y	L	Q	K	L	D	T	Cathepsin C 58-73	c
	KK	V	V	V	Y	L	Q	K	L	D	TAYD	Cathepsin C 62-76	c
	K	V	V	V	Y	L	Q	K	L	D	TAYD	Cathepsin C 63-76	c
	KP	Y	N	E	A	K	T	X	F	D	KY	Apolipoprotein B-100 3218-3230	c

* pol.: Polar; chg.: charged; ali.: aliphatic
References:
a: Friede and co-workers, submitted; b: Matsushita et al. 1994; c: Kinouchi et al. 1994

Table 6 (Continued)
G HLA-DRB1*1101

		Relative position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor residues		W,Y F			M,L V,I		R,K						a, b
Examples for ligands	IDF	Y	T	S	I	T	R	A	R	F	EE	HSC 70 291–305	b
	CPAG	Y	T	C	N	V	K	A	R	S	CEK	Granulin D 41–56	b
	VNH	F	I	A	E	F	K	R	K	H	KKD	Homol. HSC 70 238–252	b
	VNH	F	I	A	E	F	K	R	K	H	K	Homol. HSC 70 238–250	b
	MR	Y	F	H	T	S	V	S	R	P	GRGEP	HLA-Bw61 5–20	b
	KHKV	Y	A	C	E	V	T	H	Q	G	LS	Homol. Ig κ-chain 190–204	b

References:
a: Hammer et al. 1993; b: Newcomb and Cresswell 1993

H HLA-DRB1*1201

		Relative position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor residues		I,L F,Y V		L,M N,V A			V,Y F,I N,A			Y,F M,I V			a
Examples for ligands	GPDGRL	L	R	G	Y	D	Q	F	A	Y	DGK	HLA-B38 104–121	a
	GPDGRL	L	R	G	H	N	Q	Y	A	Y	D	HLA class I 104–119	a
	TGT	I	K	L	L	N	E	N	S	Y	VP	Transferrin receptor 142–155	a
	T	I	K	L	L	N	E	N	S	Y	VPR	Transferrin receptor 144–156	a
	FTGT	I	K	L	L	N	E	N	S	Y	VPR	Transferrin receptor 141–156	a
	DFTGT	I	K	L	L	N	E	N	S	Y	VPR	Transferrin receptor 140–156	a
	SDEK	I	R	M	N	R	V	V	R	N	NLR	Valosin-cont. protein p97 78–93	a
	SSV	I	T	L	N	T	N	V	G	L	YXQT	Homol. to apolipoprotein	a
	EAL	I	H	Q	L	K	I	N	P	Y	VLS	Unknown	a
	AHL	F	K	Q	N	K	V	V	H	V	NG	Dihydrolipoamide dehydrogenase 138–152	b

References:
a: Falk et al. 1994b; b: Falk and co-workers, unpublished

I HLA-DRB1*1501 (DR2b)

		Relative position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor residues		L,V I			F,Y I			I,L V,M, F					a, b
Examples for ligands	EAEQ	L	R	A	Y	L	D	G	T	G	VE	HLA-A3 152–166	a
		L	E	E	F	G	R	F	A	S	FEAQG	HLA-DRα 45–58	a
	D	V	G	V	Y	R	A	V	T	P	QGRPDA	HLA-DQw6 43–58	a
T-cell epitope	PV	V	H	F	F	K	N	I	V	T		MBP 85–95	b

References:
a: Vogt et al. 1994; b: Wucherpfennig et al. 1994

Table 6 (Continued)

K HLA-DRB5*0101 (DR2a)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		F,Y L,M			Q,V I,M					R,K			a, b
Examples for ligands	DVGV	Y	R	A	V	T	P	Q	G	R	P	HLA-DQw6 43-56	a
	DVGV	Y	R	A	V	T	P	Q	G	R	PDA	HLA-DQw6 43-58	a
	DSDVGV	Y	R	A	V	T	P	Q	G	R	PD	HLA-DQw6 41-57	a
	DSDVGV	Y	R	A	V	T	P	Q	G	R	PDA	HLA-DQw6 41-58	a
	DSDVGV	Y	R	A	V	T	P	Q	G	R	PDAEY	HLA-DQw6 41-60	a
	AAD	M	A	A	Q	I	T	K	R	K	WEAAH	HLA-A3 135-151	a
	TAAD	M	A	A	Q	I	T	K	R	K	WEA	HLA-A3 134-149	a
	DVGE	F	A	A	V	T	E	K	R	R	PDAEYW	HLA-DR2b 43-61	a
T-cell epitopes	PK	Y	V	K	Q	N	T	L	K	L	AT	HA 307-319	c
		L	Q	A	A	P	A	L	D	K	L	HSP65 418-427	a, d
	VHF	F	K	N	I	V	T	P	R	T	P	MBP 87-99	e
	ASD	Y	K	S	A	H	K	G	F	K	GVD	MBP 131-145	a
	KG	F	K	G	V	D	A	Q	G	T	LSKI	MBP 139-153	a

References:
a: Vogt et al. 1994; b: Wucherpfennig et al. 1994; c: O'Sullivan et al. 1991; d: Anderson et al. 1988; e: Martin et al. 1991

L HLA-DQA1*0501/DQB1*0301

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor residues		F,Y I,M L,V				V,L I,M Y		Y,F M,L V,I					a
Preferred residues	A		A	A	A								
Examples for ligands	TPL	L	M	Q	A	L	P	M	G	A	LPQG	Invariant chain 111-126	a
	TPL	L	M	Q	A	L	P	M	G	A	LPQ	Invariant chain 111-125	a
	KPPKPVSKMR	M	A	T	P	L	L	M	Q	A		Invariant chain 99-117	a
	LPKPPKPVSKMR	M	A	T	P	L	L	M				Invariant chain 97-115	a
	IPE	L	N	K	V	A	R	A	A	A		Transferrin receptor 579-597	a
	DVEV	Y	R	A	V	T	P	L	G	P	EVAGQF	DQβ chain 43-55	a

References:
a: Falk et al. 1994b

M HLA-DPA1*0201/DPB1*0401

		Relative position											Source	Ref.
		1	2	3	4	5	6	7	8	9	10			
Anchor residues		F,L Y,M I,V A						F,L Y,M V,I A			V,Y I,A L			a
Examples for ligands	EKK	Y	F	A	A	T	Q	F	E	P	L	AARL	Unknown	a
	KK	Y	F	A	A	T	Q	F	E	P	L	AARL	Unknown	a
	EKK	Y	F	A	A	T	Q	F	E	P	L		Unknown	a
	GPG	A	P	A	D	V	Q	Y	D	L	Y	LNVANRR	IL-3 Receptor α-chain 127-146	a

References:
a: Falk et al. 1994b

Table 6 (Continued)
N HLA-DPA1*0102/DPB1*0201

		Relative position 1	2	3	4	5	6	7	8	9		Source	Ref.
Anchor residues		F,L M,V W,Y				F,L M,Y			I,A M,V				a
Examples for ligands	ADEKKF	W	G	K	Y	L	Y	E	I	A	RRHP	Cattle serum albumin 152–170	a
	GEP	L	S	Y	T	R	F	S	L	A	RQVDG	Transferrin receptor 15–31	a
	LPSQA	F	E	Y	I	L	Y	N	K	G		Cathepsin H 185–198	a

References:
a: Rötzschke and Falk 1994

Table 7 Other human class II ligands

MHC molecule	Peptide sequence	Source		Ref.
HLA-DR2 (DRB5*0101 or DRB1*1501)	NIVIKRSNSTAATNEVPEVTVFS	HLA-DQα	97– 119	a
	NIVIKRSNSTAATNEV	HLA-DQα	97– 112	a
	SDVGVYRAVTPQGRPDAE	HLA-DQβ	42– 59	a
	DVGVYRAVTPQGRPDAE	HLA-DQβ	43– 59	
	DVGVYRAVTPQGRPD	HLA-DQβ	43– 57	
	RVQPKVTVYPSKTQPLQH	HLA-DRB1*1501	94– 111	a
	RVQPKVTVYPSKTQP	HLA-DRB1*1501	94– 108	a
	LSPIHIALNFSLDPQAPVDSHGLRPALHYQ	Fibronectin receptor α	586– 616	a
	DGILYYYQSGGRLRRPVN	K+ channel protein	173– 190	a
	IQNLIKEEAFLGITDEKTEG	Mannose binding protein	174– 193	a
	EHHIFLGATNYIYVLNEEDLQKV	MET protooncogene	59– 81	a
	QELKNKYYQVPRKGIQA	Guanylate binding protein 2	434– 450	a
	FPKSLHTYANILLDRRVPQTD	Apolipoprotein B100	1200–1220	a
	FPKSLHTYANILLDRRVPQ	Apolipoprotein B100	1200–1218	a
	LWDYGMSSSPHVLRNR	Factor VIII	1775–1790	a
HLA-DRB1*0701	RPAGDGTFQKWASVVVPSGQ	HLA-A29	234– 253	a
	RPAGDGTFQKWASVVV		234– 249	a
	GDGTFQKWASVVVPSGQEQRYT		237– 258	a
	GDGTFQKWASVVVPSGQE		237– 254	a
	GTFQKWASVVVPSG		239– 252	a
	GTFQKWASVVVPSGQ		239– 253	a
	GTFQKWASVVVPSGQEQRYTCHV		239– 261	a
	RETQISKTNTQTYRENL	HLA-B44	83– 99	a
	RETQISKTNTQTYREN		83– 98	a
	RETQISKTNTQTYRE		83– 97	a
	RSNYTPITNPPEVTVLTNSPVELREP	HLA-DR α chain	101– 126	a
	GALANIAVDKANLEIMTKRSN		58– 78	a
	SLQSPITVEWRAQSESAQSKMLSGIGGFVL	HLA-DQ α chain	179–?	a
	VTQYLNATGNRWCSWSLSQAR	4F2	318– 338	a
	VTQYLNATGNRWCSWSL		318– 334	a
	TSILCYRKREWIK	LIF receptor	854– 866	a
	PAFRFTREAAQDCEV	Thromboxane-A synthase	406– 420	a
	GDMYPKTWSGMLVGALCALAGVLTI	K+ channel protein	492– 516	a
	TPSYVAFTDTERLIGDA	Hsp 70	38– 54	a
	TPSYVAFTDTERLIG		38– 52	a
	VPGLYSPCRAFFNKEELL	EBV MCP	1264–1282	a
	VPGLYSPCRAFFNK		1264–1277	a
	KVDLTFSKQHALLCSDYQADYES	Apolipoprotein B 100	1586–1608	a
	KVDLTFSKQHALLCS		1586–1600	a
	FSHDYRGSTSHRL		1942–1954	a
	LPKYFEKKRNTII		2077–2089	a
	APVLISQKLSPIYNLVPVK	Complement C9	465– 483	a
	VGSDWRFLRGYHQYAYDG	HLA-A2	103– 120	a
	PKPPKPVSKMRMATPLLMQALP	Invariant chain	98– 119	a
	APSPLPETTENVVCALGLTV	HLA-DRα chain	182– 200	a
	KHKVYACEVTHQGL	Ig kappa chain	188– 201	a

Table 7 (Continued)

MHC molecule	Peptide sequence	Source		Ref.
HLA-DRB1*0801	APSPLPETTENVVCALG	HLA-DRα chain	182– 198	a
	SETVFLPREDHLFRKFHYLPFLP	HLA-DR α chain	158– 180	a
	RHNYELDEAVTLQ	HLA-DP β chain	80– 92	a
	DPQSGALYISKVQKEDNSTYI	LAM Blast-1	88– 108	a
	GALYISKVQKEDNSTYI		92– 108	a
	DPVPKPVIKIEKIEDMDD		129– 146	a
	DPVPKPVIKIEKIED		129– 143	a
	FTFTISRLEPEDFAVYYC	Ig κ chain	63– 80	a
	FTFTISRLEPEDFAV		63– 77	a
	DPVEMRRLNYQTPG	LAR	1302–1316	a
	YQLLRSMIGYIEELAPIV	LIF receptor	709– 726	a
	GNHLYKWKQIPDCENVK	IFN-α receptor	271– 287	a
	LPFFLFRQAYHPNNSSPVCY	IL-8 receptor	169– 188	a
	RPSMLQHLLR	Ca^{2+} release channel	2614–2623	a
	DDFMGQLLNGRVLFPVNLQLGA	CD35	359– 380	a
	IPRLQKIWKNYLSMNKY	CD75	106– 122	a
	EPFLYILGKSRVLEAQ	Calcitonin receptor	38– 53	a
	NRSEEFLIAGKLQDGLLH	TIMP-1	101– 118	a
	RSEEFLIAGKLQDGLL		102– 117	a
	SEEFLIAGKLQDGLL		103– 117	a
	NRSEEFLIAGKL		101– 112	a
	QAKFFACIKRSDGSCAWYRGAAPPKQEF	TIMP-2	187– 214	a
	QAKFFACIKRSDGSCAWYR		187– 205	a
	DRPFLFVVRHNPTGTVLFM	PAI-1	378– 396	a
	MPHFFRLFRSTVKQVD		133– 148	a
	QNFTVIFDTGSSNLWVPSVYCTSP	Cathepsin E	89– 112	a
	QNFTVIFDTGSSNLWV		89– 104	a
	TAFQYIIDNKGIDSDAS	Cathepsin S	189– 205	a
	DEYYRRLLRVLRAREQIV	Cystatin SN	41– 58	a
	EAIYDICRRNLDIERPT	Tubulin α-1 chain	207– 223	a
	EAIYDICRRNLDI		207– 219	a
	HELEKIKKQVEQEKCEIQAAL	Myosin β heavy chain	1027–1047	a
	AEVYHDVAASEFF ...	α-enolase	23–?	a
	KRSFFALRDQIPDL	c-*myc*	371– 385	a
	RQYRLKKISKEEKTPGC	K-ras	164– 180	a
	KNIFHFKVNQEGLKLSNDMM	Apolipoprotein B-100	1724–1743	a
	KNIFHFKVNQEGLKLS		1724–1739	a
	YKQTVSLDIQPYSLVTTLNS		1780–1799	a
	STPEFTILNTLHIPSFT		2646–2662	a
	TPEFTILNTLHIPSFTID		2647–2664	a
	TPEFTILNTLHIPSFT		2647–2662	a
	SNTKYFHKLNIPQLDF		2885–2900	a
	LPFFKFLPKYFEKKRNT		2072–2088	a
	LPFFKFLPKYFEKKR		2072–2086	a
	WNFYYSPQSSPDKKL		4022–4036	a
	DVIWELLNHAQEHFGKDKSKE	Cattle transferrin	261– 281	a
	DVIWELLNHAQEHFG		261– 275	a
	DVIWELLNHAQEH		261– 273	a
	IALLLMASQEPQRMSRNFVR	von Willebrand factor	617– 636	a
	IALLLMASQEPQRM		617– 630	a
HLA-DR11 or Dw52	SXVITLNTNVGLYXQS	Homol. Apolipoprotein	3345–3360	b
	DPXQDELQKLNAXDP	Unknown		b
	XPELNKVARAAAEVAG	Homol. Transferrin receptor	580– 595	b
DR17 or DRw 52	TFDEIASGFRQGGASQ	Glucose transporter	459– 474	a
	YGYTSYDTFSWAFL	Na+ channel protein	384– 397	a
	GQVKKNNHQEDKIE	CD45	1071–1084	a
	TGHGARTSTEPTTDY	EBV gp220	592– 606	a
	KELKRQYEKKLRQ	EBV tegument p140	1395–1407	a
	SPLQALDFFGNGPPVNYKTGNL	IP 30	38– 59	a

References:
a: Chicz et al. 1993; b: Newcomb and Cresswell 1993

Table 8 Mouse class II motifs

A H-2E^k

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		I,L V,F Y,W			I,L V,F S		Q,N A			K,R			a, b, c
Examples for ligands	HPPHIE	I	Q	M	L	K	N	G	K	K		β2m 42–56	c
	DNRM	V	H	F	I	A	E	F	K	R	K	HSC70 234–248	c
	TPTL	V	E	A	A	R	N	L	G	R	VG	Serum albumin 347–361	c
	VNKE	I	Q	N	A	V	Q	G	V	K	HI	C cyt inhib. 41–55	c
	GFPT	I	Y	F	S	P	A	N	K	K	L	ER60 448–461	a
	IP	L	I	M	L	I	N	K	A	R	NKAE	Unknown	a
	YDRN	T	K	S	P	L	F	V	G	K	V	α1-antitryp. 397–410	a
		F	A	E	F	G	T	L	K	K	AAVHYDRSG	Unknown	a
	LH	L	G	Y	L	P	N	Q	L	F	R	(human) dead box protein	a
	IPGGP	V	R	L	C	P	G	R	I	R		Cattle fetuin 342–	a
T-cell epitopes	RADL	I	A	Y	L	K	Q	A	T	K		MCC 91–103	b
	RADL	I	A	Y	L	K	Q	A	T	A	K	PCC 91–104	b
	LEDARR	L	K	A	I	Y	E	K	K	K		λrep 12–26	e
	QD	I	L	I	R	L	F	K	S	H	PETL	SWMb 26–40	e
	VTV	L	T	A	L	G	A	I	L	K	K	SWMb 66–78	d
		L	T	A	L	G	G	I	L	K		EqMb 69–77	b
		L	T	A	L	G	T	I	L	K		MoMb 69–77	b
		I	T	A	F	N	E	G	L	K		MoHb 68–76	b
	KVFGR	C	E	L	A	A	A	M	K	R	HGLD	HEL 1–18	e
	SALLSSD	I	T	A	S	V	N	C	A	K		HEL 81–96	d
		W	V	A	W	R	N	R	C	K	GTD	HEL 108–119	d
	VEK	Y	G	P	E	A	S	A	F	T	KKMVENAK	SNase 51–70	e
	RTDKYGRG	L	A	Y	I	Y	A	D	G	K	MVN	SNase 81–100	e
	HEHQ	L	R	K	S	E	A	Q	A	K	KEKLNIW	SNase 121–140	f
		I	A	K	F	G	T	A	F	K		LLO 218–226	b

References:
a: Schild and co-workers, submitted; b: Reay et al. 1994; c: Marrack et al. 1993; d: Spouge et al. 1987; e: Altuvia et al. 1994; F: Sette et al. 1989

B H-2E^d

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		W,Y F,I, L,V			K,R I		I,L V,G			K,R			a
Examples for ligands	SQLELR	W	K	S	R	H	I	K	E	R		IL-2R. γ chain 168–182	a
	LELR	W	K	S	R	H	I	K	E	R		IL-2R. γ chain 170–182	a
	ERAEA	W	R	Q	K	L	H	G	R	L		Apo-E prec. 222–236	a
	RAEA	W	R	Q	K	L	H	G	R	L		Apo-E prec. 223–236	a
	AQ	F	M	W	I	I	R	K	R	I	QLP	Unknown	a
	SLDEH	Y	H	I	R	V	H	L	V	K		Similar Apolipoprotein B 2211–2224	a
	GQFY	F	L	I	R	K	R	I	H	L	R	C. elegans cDNA homol. 74–87	a
	LV	V	D	N	G	S	G	M	C	K	AGF	Actin B 8–21	a
T-cell epitopes	ALWFRNH	F	V	F	G	G	G	T	K	V	TV	Ig lambda 91–108	b
	KYLEFISEA	I	I	H	V	L	H	S	R			SWM 102–118	c
	NKALE	L	F	R	K	D	I	A	A	K	Y	SWM 132–146	d
	W	V	A	W	R	N	R	C	K	G	TD	HEL 108–119	c
	A	Y	V	Y	K	P	N	N	T	H	EQHLRKSE	SNase 112–129	e
	SS	F	E	R	F	E	I	F	P	K		FLU PR/8 HA 109–119	c
	LEDARR	L	K	A	I	Y	E	K	K	K		λrep 12–26	c
	EK	I	R	L	R	P	G	G	K	K	K	HIV-1 gag p17 17–28	f

References:
a: Schild and co-workers, submitted; b: Bogen et al. 1986; c: Spouge et al. 1987; d: O'Sullivan et al. 1991; e: Chicz et al. 1992; f: Sette et al. 1989

Table 8 (Continued)

C H-2E[s]

		Relative position										Comments	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		**I,V** **L**			L,I V		Q,N			**K,R**		This motif has been predicted based on prediction of pocket structure and comparison with H-2E[k] and H-2E[d] motifs	a
												Source	
Examples for ligands		**L**	Y	V	**L**	K	I	G	K	**K**	DG	Carboxypeptidase A 44–54	b
	HPPHIE	**I**	Q	M	**L**	K	**N**	G	K	**K**		β_2 42–56	b
	EGEC	V	E	W	**L**	H	R	Y	L	**K**	NG	H-2L[d] 160–174	b
	MQKEITA	**L**	A	P	S	T	M	K	I	**K**	II	β-actin 286–303	b
	CT	F	A	I	C	W	L	P	F	**H**	VFFL	Substance P receptor 255–269	b
	EGSLI	**V**	E	K	I	M	**Q**	S	S	S	E	HSP60 478–492	b
T-cell epitope	DL	**I**	A	Y	**L**	K	**Q**	A	T	**K**		MCC 93–103	c, d

References:
a: Schild and wo-workers, submitted; b: Marrack et al. 1993; c: Altuvia et al. 1994; d: Reay et al. 1994

D H-2E[b]

		Relative position										Comments	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		**W,F** **Y**			L,I F,V		Q,N, A			**K,R**		This motif has been predicted based on prediction of pocket structure and comparison with H-2E[k] and H-2E[b] motifs	a
												Source	
Examples for ligands	SPSYV	**Y**	H	Q	**F**	E	R	R	A	**K**	YK	MuLV env protein 454–469	b
	SPSYV	**Y**	H	Q	**F**	E	R	R	A	**K**	YKREPVSL	MuLV env protein 454–475	b
	SPSYV	**Y**	H	Q	**F**	E	R	R	A	**K**		MuLV env protein 454–467	b
	GK	**Y**	L	Y	E	I	**A**	R	R	**H**	PYFY	BSA 141–155	b
	XPQS	**Y**	L	I	H	E	X	X	X	I	S	Unknown	b
T-cell epitopes	RTDKYGRG	**L**	A	Y	I	Y	**A**	D	G	**K**	MVN	SNase 81–100	c, d
	DL	**I**	A	Y	L	K	**Q**	A	T	**K**		MCC 93–103	c, d

References:
a: Schild and co-workers, submitted; b: Rudensky et al. 1991; c: Altuvia et al. 1994; d: Reay et al. 1994

Table 9 Other mouse class II ligands

MHC Molecule	Peptide sequence	Source		Ref.
H-2A[b]	HNEGFYVCPGPHRP	MuLV env	145-158	a
	ASFEAQGALANIAVDKA	H-2Eα	52- 68	a
	KPVSQMRMATPLLMR	Invariant chain	86-100	a
	NYNAYNATPATLAVD	Unknown		a, b
	RPDAEYWNSQPE	H-2Aβ	55- 66	b
	XNADFKTPATLTVDKP	IgG V_μ	59- 74	b
H-2A[s]	IRLKITDSGPRVPIGPN	MuLV env	255-269	b
	IRLKITDSGPRVPIG	MuLV env	255-267	b
	WQSQSITCNVAHPASST	IgG2a	194-210	b
	NVEVHTAQTQTHREDY	IgG2a	281-296	b
	KPTEVSGKLVHANFGT	Transferrin receptor	203-218	b
	XPYMFADKVVHLPGSQ	Unknown		b
H-2A[d]	WANLMEKIQASVATNPI	Apo-E	268-284	c
	WANLMEKIQASVATNP	Apo-E	268-283	c
	DAYHSRAIQVVRARKQ	Cys-C	40- 55	c
	ASFEAQGALANIAVDKA	H-2I-Eα[d]	52- 68	c
	ASFEAQGALANIAVDK	H-2I-Eα [ed]	52- 67	c
	EEQTQQIRLQAEIFQAR	Apo-E	236-252	c
	EQTQQIRLQAEIFQAR	Apo-E	237-252	c
	KPVSQMRMATPLLMRPM	Li	85-101	c
	VPQLNQMVRTAAEVAGQX	Tf recp.	442-459	c
	ISQAVHAAHAEINE	Ovalbumin	323-336	c
	LEDARRLKAIYEKKK	λ repressor	12- 26	c
H-2A[k]	DGSTDYGILQINSR	Hen egg lysozyme	48- 61	d
	DGSTDYGILQINS		48- 60	d
	DGSTDYGILQINSRW		48- 62	d
	DYGILQINSRWW (C)		52- 63 (64)	d
	IIANDQGNRTTPSY	hsp70	28- 41	d
	TPRRGEVYTCHVEHP	H-2I-A[k] β chain	165-179	d
	KVHGSLARAGKVRGQTPKVAKQ	S30 ribosomal protein	75- 96	d
	AGKVRGQTPKVAKQEKKKKKT		83-103	d
	EPLVPLDNHIPENAQPG	Ryudocan	84-100	d
	XQLGAQNEMLXPL	Unknown		e
	XXKKGTDFQLNQLE	Transferrin	100-113	e
	KGTDFQLNQLEGKKG	Transferrin	103-117	e
	YVRFDSFVGEYRAVT	H-2Aβ[k]	37- 51	e
	XPLALQFAELPVNKG	Unknown		e
	XNLRFDSDVGEFRAV	H-2Eβ[k]	33- 47	e
	EDENLYEGLNLDDXSMYE	MBI	177-194	e
	XXLYNKGIMGEdSYPY	Cathepsin H	77- 92	e
	SYLDAXVXEQLAT	Fcε-Receptor II	298-310	e
	XXXHFVHQFQPFcyF	H-2Aβ[k]	3- 17	e
	QFQPFXYFTNT	H-2Aβ[k]	10- 20	e
H-2A[g7]	KPKATAEQLKTVMDD	Serum albumin	560-574	f
	GHNYVTAIRNQQEG	Transferrin	55- 68	f
	ETTEESLRNYYEQ	hnRNP B1 & A2	31- 43	f
	VVMRDPASKRSRGFGF	hnRNP A2 & B1	51- 66	f
	VVMRDPQTKRSRGFGF	hnRNP A1	44- 59	f
	PKEPEQLRKLFIGGL	hnRNP A1	7- 21	f
	VVYPWTQRYFDSF	β Globin major	33- 45	f

References:
a: Rudensky et al. 1991; b: Rudensky et al. 1992; c: Hunt et al. 1992b; d: Nelson et al. 1992; e: Marrack et al. 1993; f: Reich et al. 1994

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